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Asian Venous Forum**



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Asian Society for Vascular Surgery
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The Annals of Vascular Diseases is an emerging journal launched from Japan in 2007.

The Journal publishes peer-reviewed original articles, editorials, reviews, case reports and others in vascular research, vascular medicine, surgery, and the allied fields. Several journals dedicated to the vascular field exist in Asia including Japan. The **Japanese College of Angiology**, the **Japanese Society for Vascular Surgery** and the **Japanese Society of Phlebology**, therefore, collaborated to sponsor this new journal to jump-start the development and maturity of this growing field. Since October 2008 and June 2010, AVD has been the Official Journal of Asian Society for Vascular Surgery and Asian Venous Forum as well respectively.

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The Annals of Vascular Diseases (AVD) publishes Review Articles, Original Articles, Case Reports, How to Do It, Editorials (invited), other Invited Articles, and others in the field of vascular research, medicine and surgery. All manuscripts are peer-reviewed.

Although the publication of AVD is financially supported by Japanese College of Angiology, The Japanese Society for Vascular Surgery and Japanese Society of Phlebology, submission to AVD is not only limited to the members of the Societies but open for all non-member of the Societies. The submission to AVD is welcomed not only from Japanese but also from Asian countries and elsewhere.

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2. Roos DB. Transaxillary first rib resection for thoracic outlet syndrome. In: Bergan JJ, Yao JST eds. *Operative Techniques in Vascular Surgery*. New York: Grune and Stratton, 1980: 125–9.

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➤ **Special Article Series: Diagnostic Imaging** ◀

Progress and Current State of Coronary CT

Masahiro Jinzaki, MD,¹ Yutaka Tanami, MD,¹ Minoru Yamada, MS,² and Sachio Kuribayashi, MD¹

The recent appearance of multislice computed tomography (CT) has enabled noninvasive imaging of the coronary artery. Particularly, the appearance of 64-row CT has rapidly promoted its spread into routine medical practice. In this report, progress and current state of coronary CT employing multislice CT are outlined.

APPEARANCE AND PROGRESS OF MULTISLICE CT

Temporal, spatial, and contrast resolutions are essential factors that help us determine the quality of computed tomography (CT) images. To visualize the coronary arteries composed of rapidly moving small sized vessels, all these resolutions should be high. There had been many attempts to observe the coronary artery by helical CT, but both temporal and spatial resolutions were insufficient, and the attempts were rather investigative. The ultra-fast CT was anticipated very much, but contrast resolution was insufficient. The progressive development of multislice CT enabled the clinical application of coronary CT, to which the following 3 advancements contributed to 1) an increase in the number of detector rows, 2) an increase in the speed of gantry rotation, and 3) the development of an image reconstruction method exclusive for the heart.

1) Increase in the number of detector rows

Conventional helical CT was capable of acquiring only one image per rotation. The acquisition of several images per rotation was achieved by increasing the number of detector rows in the axial direction in multislice

CT, which simultaneously realized an increased speed (improvement of temporal resolution) and acquisition of thin slices (improvement of spatial resolution). In 1998, 4-slice CT capable of simultaneously acquiring data from 4 slices appeared, and it could acquire 1–1.25-mm slices of the heart in 40 seconds. Sixteen-slice CT, capable of acquiring 0.5–0.625-mm slices of the heart in 20 seconds, appeared in 2002, and 64-slice CT, capable of acquiring 0.5–0.625-mm slices in 5–7 seconds, appeared in 2004.

2) Increased speed of gantry rotation

Faster gantry rotation is necessary to increase the temporal resolution of coronary CT. The gantry rotation speed of conventional helical CT was 1 second, but CT with a speed of 0.8 seconds appeared in 1996. The speed was improved to 0.5 seconds in 2001 in which 16-slice CT appeared, and a speed of 0.35 seconds (temporal resolution: 175 msec) was realized in 2004.

3) Development and progress of an image reconstruction method exclusive for the heart

Electrocardiographic gating is necessary to image the heart because it constantly beats. There are 2 methods to perform an electrocardiography-gated scan in multislice CT: 1) prospective gating, in which radiation is emitted only in a specific cardiac phase beforehand, and 2) retrospective gating, in which electrocardiographic and imaging information is simultaneously collected, and data on the target cardiac phase is extracted and reconstructed into an image.

On extraction of the target cardiac phase in retrospective gating, when the heart rate is 65 bpm or less and the R-R interval is long, an image can be prepared from data of a single heartbeat by collating with, for example, the

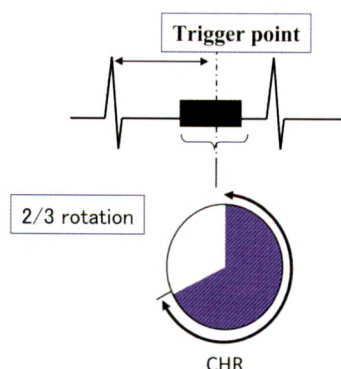
¹Department of Diagnostic Radiology, Laboratory in Research Park, Keio University School of Medicine, Tokyo, Japan

²Department of Cardiovascular Imaging, Laboratory in Research Park, Keio University School of Medicine, Tokyo, Japan

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Corresponding author: Masahiro Jinzaki, MD. Department of Diagnostic Radiology, Keio University School of Medicine, 35 Shinano-machi, Shinjuku-ku, Tokyo 160-0016, Japan
Tel: +81-3-3353-1211, Fax: +81-3-3225-5715
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Cardiac Half Reconstruction (40~65bpm)



Multi Sector Reconstruction (> 65bpm)

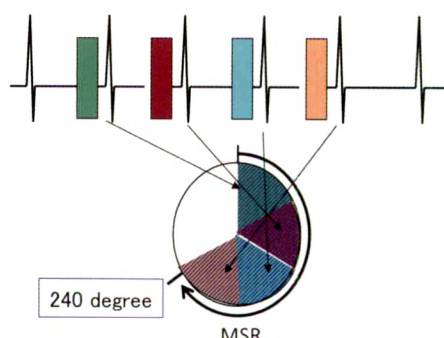


Fig. 1 Electrocardiographic gating.

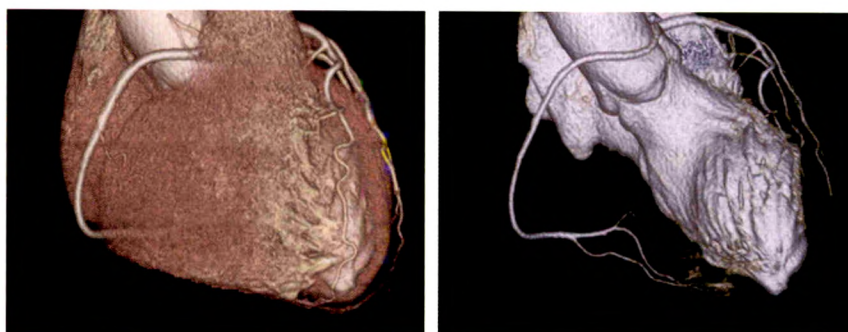


Fig. 2 CT image of single coronary artery.
The right coronary artery branched from the left coronary cusp.
CT, computed tomography

mid-diastolic phase (Fig. 1). However, when the heart rate is high, the R-R interval is short, if an image is reconstructed from data of a single heartbeat, resulting in poor image quality, for which a method to reconstruct an image by extracting and combining data of the same phase from several consecutive heartbeats was developed. This method is called multi-sector reconstruction (the name differs among manufacturers). This method increased temporal resolution and facilitated application for cases with a high heart rate.

CURRENT STATE AND PROBLEMS OF CORONARY ARTERIAL EXAMINATION EMPLOYING 64-ROW CT

Current coronary CT is capable of providing information concerning the anatomical distribution of the coronary artery, diagnosis of coronary arterial stenosis, and

coronary arterial wall evaluation.

Of these, the most firmly established usefulness is exhibited in identifying the anatomical distribution of the coronary arteries. Reportedly, abnormal origins of the coronary artery, single coronary artery, and coronary arteriovenous fistula are accurately visualized, compared to angiography (Fig. 2).^{1, 2)} It is very useful to perform percutaneous coronary intervention (PCI) if information on the abnormal origin of the coronary artery is available beforehand.

The diagnostic performance of the detection of coronary arterial stenosis is very high: both the sensitivity and specificity of 64-detector CT were between 90% and 95%, and the accuracy of detecting negativity was reported to be close to 100% (Table 1, Fig. 3).³⁻⁶⁾ Thus, 64-detector CT has been employed to detect coronary arterial stenosis in patients suspected of having ischemic heart disease. For the analysis of stenosis, a new image

Table 1 Diagnostic performance of 64-slice CT for the detection of significant coronary stenosis (>50%)

Per-segment	N	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Leschka et al	67	94	97	87	99
Leber et al	55	76	97	75	97
Raff et al	70	86	95	66	98
Mollet et al	51	99	95	76	99
Ropers et al	81	93	97	56	100
Schuijf et al	60	85	98	82	99
Ong et al	134	82	96	79	96
Ehara et al	69	90	94	89	95
Nikolaou et al	72	82	95	69	97
Weustink et al	77	95	95	75	99
Leber et al	88	94	99	81	99
Total	824	89	96	78	98

Schroeder et al. Eur Heart J 2008; 29: 531–56.⁶⁾

N, number; PPV, positive predictive value; NPV, negative predictive value

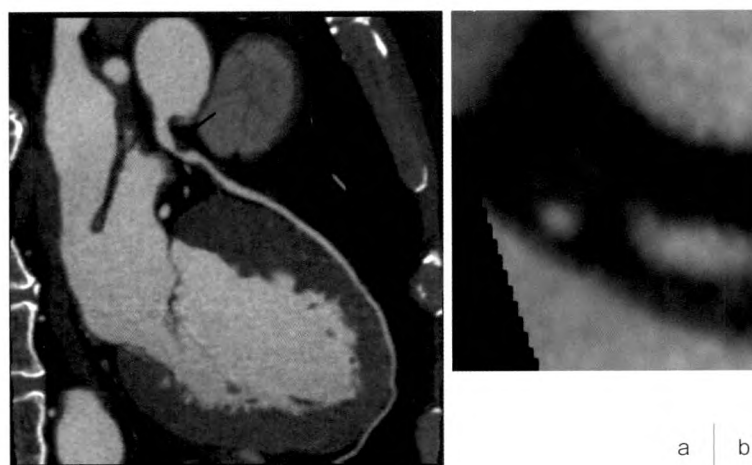


Fig. 3 CT image of coronary arterial stenosis.

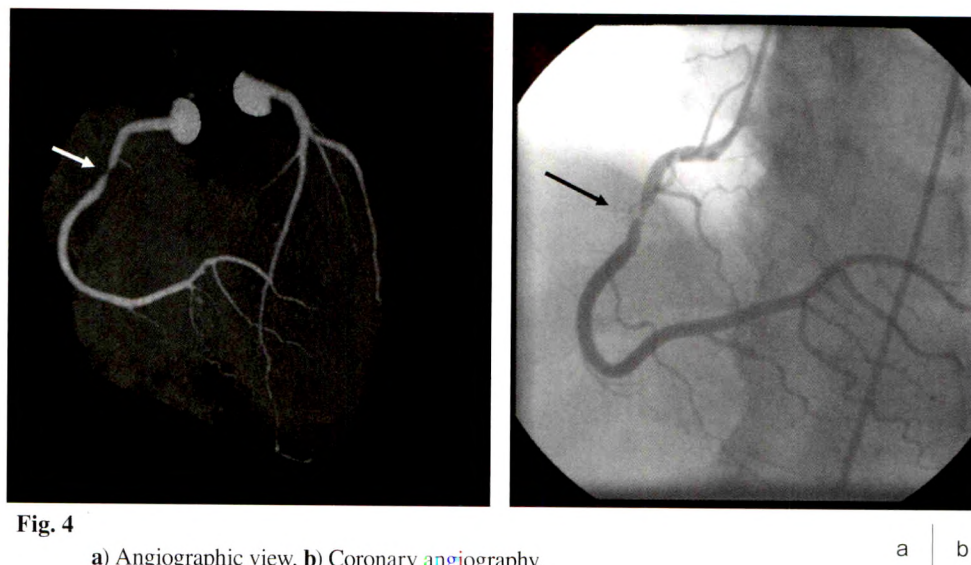
a) Curved MPR, b) Cross-sectional view: An eccentric plaque is present at the site marked with an arrow.

CT, computed tomography; MPR, multiplanar reconstruction

display method to display the distribution of lesions in a single image, an angiographic view, has been developed and effectively used for explaining the severity of disease to patients and designing treatment plans (**Fig. 4**).^{7, 8)}

To consider the treatment policy and prognosis of ischemic heart disease patients, we judge the presence or absence of myocardial infarction as being more important than that of coronary artery stenosis. It was reported that abnormal perfusion was present on single-photon emission computed tomography (SPECT) in only about half of patients in whom significant stenosis was observed on coronary CT.⁹⁾ In the deferral of percutaneous coronary intervention (DEFER) study, a pressure

wire was inserted into intermediate stenosis lesions in which the significance of stenosis was unclear on coronary angiography. The fractional flow reserve (FFR), representing the functional severity of coronary stenosis, was calculated from the intracoronary pressure measurement, and the outcome of PCI was investigated. This study revealed that the FFR value is important for the outcome of PCI, rather than the degree of stenosis.¹⁰⁾ Although the diagnostic performance of coronary CT for the detection of morphological stenosis is high compared to coronary angiography, it does not necessarily predict functionally significant stenosis, i.e., ischemia. Evaluation of myocardial perfusion by loading a drug (adenosine

**Fig. 4**

a) Angiographic view, b) Coronary angiography.

Significant stenosis is observed in the right proximal coronary artery, showing a similar view to that on coronary angiography.

triphosphate (ATP) or adenosine) and myocardial staining in the early phase has recently become possible, and this CT perfusion has recently been investigated.^{11, 12)}

As differences between myocardial blood flow information and morphological information of the coronary artery have been clarified, CT/SPECT fusion images have been increasingly used, in which evaluations of coronary arterial stenosis and the myocardial blood flow reserve estimated by SPECT were integrated (Fig. 5).^{13, 14)} Myocardial SPECT is capable of collecting functional information, such as myocardial blood flow and metabolism, and extensive evidence concerning the diagnosis, judgment of treatment, prognosis, and course observation of ischemic heart disease has been accumulated. CT/SPECT fusion images share advantages of morphological and functional images, which is useful for the investigation of ischemic regions, evaluation of myocardial ischemia in each coronary arterial branch, and identification of the responsible blood vessel.

It was expected that CT provides information for coronary arterial wall evaluation, surpassing that provided by coronary angiography. The coronary arterial wall is evaluated based on the plaque properties and volume. Regarding the diagnosis of plaque properties, a study on comparison with intravascular ultrasound (IVUS) reported that CT values of 50 HU or lower and 50–120 HU indicated the dominance of lipids and fiber, respectively, and 120 or HU indicated calcification,¹⁵⁾ which generated much expectation. However, the CT value of

plaques varied due to the influence of the concentration in the coronary arterial lumen,¹⁶⁾ and the prediction of unstable plaques based on the CT values became considered difficult. Later, a study reported that the risk of acute coronary syndrome (ACS) is high when the plaque is accompanied by all of the following 3 factors: a CT value of 30 HU or lower (low-density plaque), positive remodeling, and spotty calcification.¹⁷⁾ A prospective study on whether or not the CT values of plaques serve as a predictor of vascular events is currently underway, and the results are anticipated. Regarding plaque volume evaluation, data showing a relatively strong correlation with IVUS have been reported,¹⁸⁾ but further improvement of the accuracy may be necessary.

Problems of 64-slice CT are as follows: 1) poor image quality possibly from motion artifacts in patients with arrhythmia and a high heart rate, 2) incomplete presentation of the vascular lumen for the evaluation of stenosis when artifacts of calcification are present in many severely calcified lesions, 3) insufficient accuracy for routine use because of overestimated or underestimated plaque volumes,⁴⁾ 4) dependence of CT values of plaques on those of the vascular lumens for diagnosing plaque properties, and 5) difficulty in the evaluation of stent lumen less than 3mm due to artifact. Coronary CT may be less useful than conventional coronary angiography for follow-up after PCT because the evaluation of thin stents is difficult. The improvement of spatial and temporal resolutions is expected to overcome these problems.

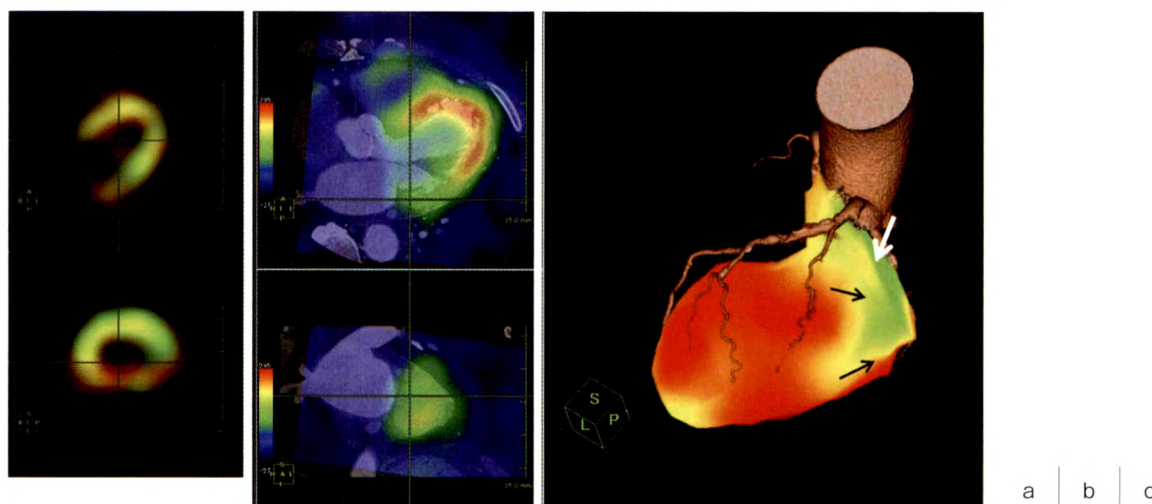


Fig. 5 CT/SPECT fusion image.

SPECT images (a) were fused with cardiac CT images (b) to display a 3-dimensional image (c).

The proximal circumflex branch shows 99% stenosis (c: white arrow), and reduced perfusion (→) in its distributed region can be readily perceived.

CT, computed tomography; SPECT, single-photon emission computed tomography

POSITIONING OF CORONARY CT IN THE GUIDELINES

There are several guidelines for the application of coronary CT. In Western countries, guidelines have been prepared since around 2006, and the clinical efficacy and validity of indications of cardiac CT and magnetic resonance (MR) have been discussed.^{6, 19–22)} The guidelines for cardiac CT prepared by the Asian Society of Cardiovascular Imaging were established to correspond to the state in Asia.²³⁾ The Society of Cardiovascular Computed Tomography prepared guidelines concerning the test method and interpretation of images of cardiac CT, which did not include the indication or efficacy.^{24, 25)}

In Japan, the Japan Circulation Society published the 2007–2008 joint study group report ‘Guidelines concerning noninvasive diagnostic methods of coronary arterial lesions’ in 2009,²⁶⁾ which contain most integrative contents, reviewing the following test methods and discussing their positions in the evaluation of coronary arterial lesions: 1) resting electrocardiography, 2) exercise electrocardiography, 3) echocardiography, 4) nuclear medical test of the heart, 5) coronary CT, and 6) cardiac MR. The positioning of coronary CT with regard to stable angina pectoris, acute coronary syndrome, and follow-up of PCI in these guidelines is introduced below.

1) Cases suspected to be stable angina pectoris

When patients with chest pain are first examined, the absence of unstable angina pectoris should be confirmed from the clinical symptoms. The possibility of coronary arterial disease is then assumed based on age, gender, and symptoms (Duke Database), and a decision on the diagnostic policy should be made. When the risk of coronary arterial disease is low, course observation is sufficient. When the risk is high, coronary angiography is applied. In cases other than these, noninvasive tests are performed, for which exercise electrocardiography is recommended because it is simple and cost-effective, and exercise tolerability and the prognosis can also be evaluated. Patients are classified into low-, intermediate-, and high-risk groups based on the findings (Fig. 6-1). When the patient cannot perform exercise or electrocardiographic diagnosis is impossible, cardiac CT or myocardial perfusion scintigraphy is directly performed (Fig. 6-2).

In the high-risk group, the possibility of having a coronary arterial disease is high, and it is difficult to rule out, even if no significant stenosis is detected by coronary CT. Thus, coronary angiography is immediately performed in many cases. Coronary CT may be useful to predict the no-reflow phenomenon and applicability of PCI in some cases even though they are being classified into the high-risk group.^{27, 28)} For the low-risk group, the necessity of coronary CT is low because the prevalence of coronary arterial disease is low.

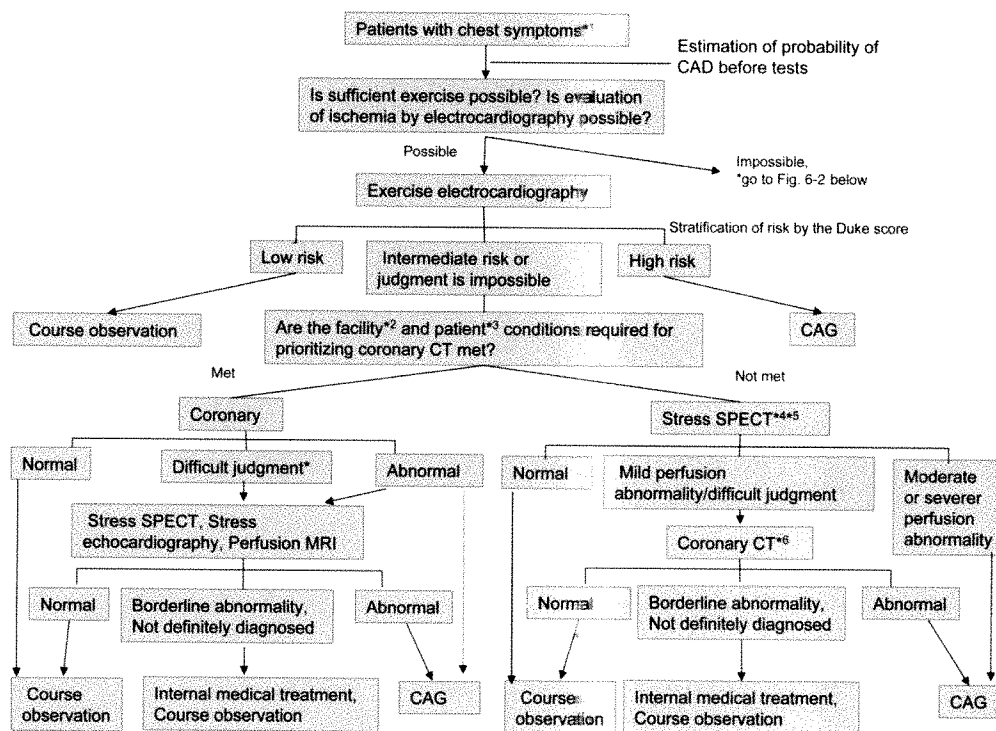


Fig. 6-1 Diagnostic tree of stable angina pectoris: When exercise is possible (for explanation, refer to the text).

Cited from *Circulation Journal Vol.73. Supple. 1H, 2009, 1091–114.*

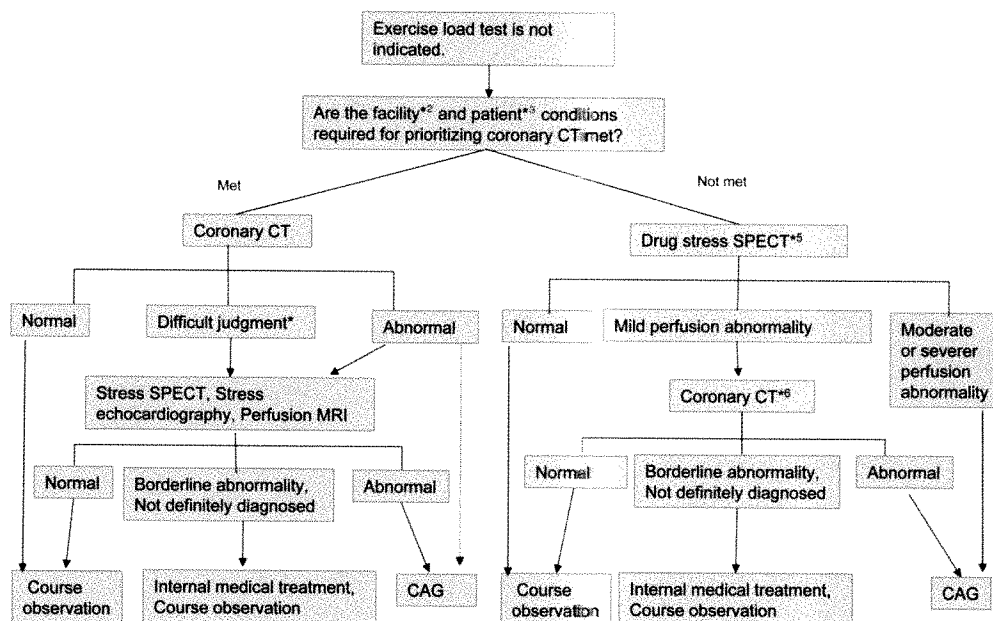


Fig. 6-2 Diagnostic tree of stable angina pectoris: When exercise is not possible (for explanation, refer to the text).

Cited from *Circulation Journal Vol.73. Supple. III, 2009, 1091–114.*

*1: Asymptomatic patients strongly suspected of having coronary arterial disease based on electro- and echocardiography findings are included.

*2: Desirable facility conditions for prioritizing coronary CT

- Sufficient experience
- Equipped with a 64-row or higher model MDCT
- Operation of an appropriate reporting system of clear images

- Evaluation of CT characteristics based on comparison with CAG

- Coping with an exposure-reducing protocol

*3: Patient conditions to apply coronary CT

- Consideration of exposure is necessary for females younger than 50 years of age
- Marked coronary arterial calcification is not expected (dialysis and elderly patients)

- A serum creatinine level lower than 2.0 mg/dL

- eGFR higher than 60 mL/min/1.73 m²
- The absence of nephropathy including microalbuminuria in diabetic patients

- The absence of allergy to contrast media

- The absence of asthma

*4:

- Exercise loads are desirable.

- The summed stress score is determined employing the 17- or 20-segment method.

*5:

- Caution is necessary for contraindicated drugs.

- Stress echo or stress perfusion MRI depending on the facility

*6: Facility requirements to perform coronary CT

- Sufficient experience
- Equipped with a 64-row or higher model MDCT

* Difficult judgment

- Difficulty in making a judgment due to severe calcification and motion artifact

- Borderline stenosis and stenosis of a thin peripheral branch

CT, computed tomography; MDCT, multidetector-row CT; CAG, coronary angiography; CAD, coronary artery disease; MRI, magnetic resonance imaging system

For the intermediate-risk group or when judgment is impossible, myocardial perfusion scintigraphy or coronary CT is selected in consideration of the facility (such as sufficient experience in cardiac CT) and patient (such as iodine allergy and renal function) conditions. Since NVP of cardiac CT is high, when no significant stenosis is observed on cardiac CT, coronary arterial disease can be mostly ruled out, showing that coronary CT is sufficiently useful to examine this group. When coronary CT findings are normal, the probability of the presence of coronary arterial lesions is low, and course observation is sufficient. In contrast, when judgment by coronary CT is difficult (due to severe calcification and motion artifacts) or when a lesion indicating significant stenosis is present, it is important to investigate ischemia employing myocardial perfusion scintigraphy. Invasive coronary angiography is performed when severe ischemia requiring revascularization is predicted from the stenosis lesion.

2) Cases suspected to be acute coronary syndrome

Several studies reported a high diagnostic performance of 64-slice CT for acute coronary syndrome.²⁹⁻³⁴⁾

The risk of acute coronary syndrome is stratified with clinical findings including the age and gender, past medical history, new electrocardiographic changes, and blood chemistry (myocardial markers, such as troponin). When the risk, i.e., the possibility of acute myocardial infarction, is judged to be high, these patients are first admitted to the intensive care unit, the performed coronary angiography and revascularization. For intermediate- and low-risk groups and cases in which acute coronary syndrome cannot be definitely diagnosed because of the absence of electrocardiographic and blood test abnormalities on admission, coronary CT early after arriving at the hospital has become considered useful for the early diagnosis or diagnosis by exclusion of acute coronary syndrome, by which invasive coronary angiography can be avoided. It is controversial for the low-risk group, but many physicians consider that coronary CT is useful for reliably ruling out acute coronary syndrome.

Invasive reperfusion therapy was established as acute-phase treatment of ST-segment elevated acute myocardial infarction, for which a rapid, accurate diagnosis is necessary, and not much time should be devoted to noninvasive imaging diagnosis. Coronary CT is not used as a rule because the decrease is definitely diagnosed by electrocardiography and echocardiography, followed by coronary angiography.

3) Follow-up after PCI

In Japan, coronary angiography is habitually performed 0.5–1 year after PCI at many facilities. The main purposes are 1) evaluation of the coronary arterial lumen at the treated site, and 2) evaluation of patency of the coronary artery stent.

Although there has been no report on the diagnostic CT results for coronary arterial lumens at sites treated with POBA, DCA, and rotator, it may be appropriate to consider that the diagnostic performance of CT for these sites is similar to that for conventional significant coronary arterial stenosis lesions because no device is left in the site after treatment employing these techniques. Evaluation of rotator-treated sites may be difficult due to residual calcification, even after treatment.

Generally, the stent lumen can be evaluated by coronary CT when the stent diameter is 3 mm or larger, but the appearance varies depending on the stent type and material, and various artifacts are likely to appear on CT of pulsating thin metal stents. In a study employing 64-slice CT, the lumen could be evaluated in about 60% of stents, and the sensitivity and specificity in the group in which the lumen could be evaluated were 86 and 98%, respectively.³⁴⁾ Evaluation was possible in 85% of stents with a diameter of 3 mm or larger, but only 26% of stents with a diameter smaller than 3 mm, for which CT is not indicated.¹⁹⁾ Therefore, at present, the evaluation of stent patency by CT is limited.

4) Evaluation of bypass graft and its anastomosed site

CT is relatively useful for evaluation after coronary artery bypass grafting (Fig. 7). Evaluation items after grafting include graft patency and the presence or absence of stenosis of anastomosed sites and stenosis lesions in the native artery. In a meta-analysis of graft evaluations, the diagnostic sensitivity and specificity of occluded lesions were 97.6% and 98.5%, respectively, and evaluation was possible in 96% of grafts, while those of stenosis lesions were 88.7% and 97.4%, respectively, and evaluation was possible in 88% of grafts.³⁵⁾ In another meta-analysis, in which exclusion criteria was not set, the diagnostic performance of detecting graft patency (occlusion and stenosis) in 78%–100% of grafts were sensitivity, 97.6%; specificity, 96.7%; positive prediction rate, 92.7%; and negative prediction rate, 98.9%.³⁶⁾ These reports indicate that 64-slice CT is a useful modality for diagnosis of the patency of anastomosed regions entirely covering the graft.

Regarding evaluation of the native artery by CT, evaluation of the distal anastomosed site is difficult due to



Fig. 7 CT images after CABG.
a) Volume-rendering image after CABG, b) Curved MPR image of RITA-LAD, c) Curved MPR image of LITA-4AV-4PD, d) Curved MPR image of GEA-4PD.
No stenosis or occlusion is present in any bypass.
CABG, coronary artery bypass graft; RITA-LAD, right internal thoracic artery-left anterior descending coronary artery; GEA-4PD, gastroepiploic artery-4 posterior descending artery

a	b	c
	d	

the presence of a thin diameter in many cases. Moreover, many cases with complex lesions for which PCI is unsuccessful, complicating diabetes, multivessel lesions, and advanced atherosclerosis are included in CABG-treated cases, and these conditions make evaluation difficult. Ropers et al. reported that 9% of segments could not be evaluated, and the sensitivity and specificity were 86% and 76%, respectively, as the diagnostic performance for detecting significant stenosis lesions in the evaluable segment cases.³⁷⁾

TRANSITION FROM COMPETITION FOR INCREASING THE NUMBER OF DETECTOR ROWS TO RADIATION DOSE REDUCTION

After the appearance of 64-slice CT, competition for increasing the number of detector rows came to an end, and manufacturers began to compete to develop exposure-reducing techniques. Consciousness of exposure

reduction is important. In addition to making efforts to avoid unnecessary tests, exposure in clinically significant tests should also be minimized. The exposure level in chest CT employed for conventional lung screening (non-electrocardiography-gated high-pitch helical scan) is about 7 mSv, whereas the attenuation level in cardiac CT employing the standard cardiac helical method (low-pitch electrocardiography-gated helical scan) reaches 13–15 mSv in men and 18–21 mSv in women.³⁸⁾ These are higher than in cardiac catheterization (3–6 mSv). The risk of X-ray attenuation-induced carcinogenesis in the mammary gland and lung is not negligible at these levels, and it is particularly problematic for young women, for which a dose-reducing acquisition method was developed (Fig. 8).

A method to reduce the radiation dose in systole, called ECG modulation, was initially developed (Fig. 8b).³⁹⁾ In this method, the systolic-phase radiation dose was decrease to about 20% compared with that of the

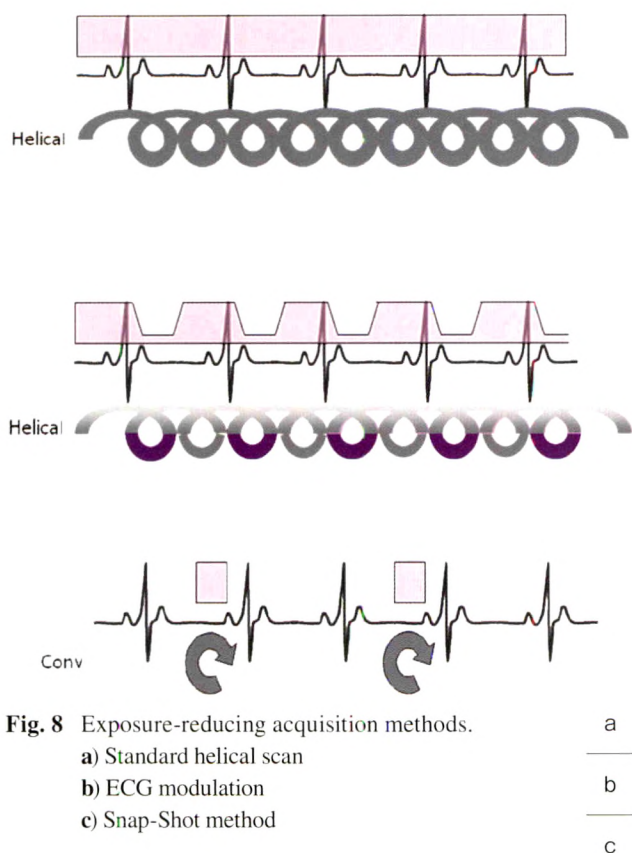


Fig. 8 Exposure-reducing acquisition methods.
 a) Standard helical scan
 b) ECG modulation
 c) Snap-Shot method

diastolic-phase, because the systolic phase data is not usually used; therefore, the dose of exposure was reduced by about 40%–59%. Later, a method involving X-ray irradiation only in mid-diastolic phase and data collection by repeating the axial scan (SnapShot Pulse method) was developed (**Fig. 8c**). The SnapShot Pulse method reduced the dose to about 1/3–1/4 because there is no irradiation in the cardiac phase excluding mid-diastolic phase.⁴⁰⁾ Application of this method is difficult for cases with a 70-bpm or higher heart rate, but stable, marked reduction of exposure is possible when the heart rate is 70-bpm or less. The active application of these methods by reducing the heart rate through the β -blocker administration is recommended.

In addition, a method called Adaptive Statistical Iterative Reconstruction (name varies between manufacturers) applying the concept of successive approximations has recently been developed, further promoting exposure reduction.⁴¹⁾

POST-64-SLICE GENERATION CT

After 2006, post-64-slice generation CT appeared, such as 320-row CT (Aquilion One, Toshiba), 256-row

CT (Brilliance iCT, Philips), dual source CT (SOMATOM Definition, Siemens), and Gemstone CT (Discovery CT 750HD, GE). These aimed at increasing temporal and spatial resolutions; however, the new technique dual energy CT has now been introduced.

1) Increase in temporal resolution and shortening of acquisition time

Toshiba and Philips further increased the number of detector rows, but there was no extension of the previous attempt to increase the number of detector rows, and they were differently positioned, called area detector CT, to image the heart on a single rotation without helical acquisition. It is applicable for patients with arrhythmia and a high heart rate because the acquisition time is short, attracting attention. Since the entire heart is simultaneously imaged, it may be useful for CT perfusion. Toshiba performed an international joint study on CT perfusion, named Core 320, using Aquilion One. Brilliance iCT of Philips realized high-speed rotation (0.27 seconds) by adopting the air-bearing method.

Siemens achieved 83-msec temporal resolution by equipping 2 tubes with a rotation speed of 330 msec (SOMATOM Definition). A model with an increased rotation speed (280 msec) and temporal resolution (75 msec) has also been marketed (SOMATOM Definition Flash). In this model, the table movement speed was increased 12–30 times, and 2 pairs of X-ray tubes and detectors simultaneously collect data in 2 spiral tracks, through which high-pitch (pitch: 3.2) acquisition is possible. The entire heart is imaged within about 0.25 seconds, facilitating scan time and exposure reduction.

2) IMPROVEMENT OF SPATIAL RESOLUTION

The width of detector rows in the axial direction is 0.5–0.6 mm in current models of CT. Discovery CT 750HD, marketed by GE last year, is equipped with detectors in which the molecular structure of garnet was adopted for the scintillator. The response to X-rays was increased 100 times and afterglow was reduced to 1/4 in this garnet detector (Gemstone) compared to the previous detector. Using this detector, we can sample high-speed data, and, subsequently, the number of views can be increased to about 2.5 times of that on previous 64-row CT. The spatial resolution of the XY planes increases as the number of views increases. In our study, spatial resolution was increased by about 30%, and the diagnostic performance for stents with a 3-mm or smaller diameter was improved (**Fig. 9**).



Fig. 9 CT image of a stent with a diameter smaller than 3 mm.

Curved MPR image, CAG image.

a) The stent is imaged using a large number of views, and patency of the 2.5–3-mm stent lumen can be observed.

b) Patency was confirmed by CAG.

CT, computed tomography; MPR, multiplanar reconstruction; CAG, coronary angiography

3) Dual energy CT

In the dual energy method, images are acquired at 2 tube voltages (for example, 80 and 140 kV), not at the standard single tube voltage (for example, 120 kV). The CT value of substances varies depending on the tube voltage, and the rate of CT value change between the 2 tube voltages varies among substances. When CT value data at 2 tube voltages are available, the discrimination of substances, for example, iodine and calcification, is possible. Using the dual energy method, the separation of calcium (calcified plaque) from iodine (vascular lumen) is theoretically possible in blood vessels with difficulty in evaluating the stenosis rate due to severe calcification.⁴²⁾ If the stenosis rate of severely calcified lesions could be accurately determined employing the dual energy method, it would be very useful, leading to expansion of the indication of cardiac CT.

At present, dual source CT (Siemens) and garnet detector CT (GE) are capable of dual energy scanning, but only dual source CT is capable of electrocardiographic gating. It may be equipped with garnet detector CT (GE) in the coming year.

CONCLUSION

The progress of CT was outlined from the appearance of multislice CT, through to competition to increase the number of detector rows, dose reduction, and post 64-slice CT. We expect further progress in the reconstruction method, development of detectors, and reduction of exposure, facilitating that evaluation of diverse functions.

REFERENCES

- 1) Datta J, White CS, Gilkeson RC, Meyer CA, Kansal S, Jani ML, et al. Anomalous coronary arteries in adults: depiction at multi-detector row CT angiography. *Radiology* 2005; **235**: 812–8.
- 2) Schmid M, Achenbach S, Ludwig J, Baum U, Anders K, Pohle K, et al. Visualization of coronary artery anomalies by contrast-enhanced multi-detector row spiral computed tomography. *Int J Cardiol* 2006; **111**: 430–5.
- 3) Leber AW, Knez A, von Ziegler F, Becker A, Nikolaou K, Paul S, et al. Quantification of obstructive and non-obstructive coronary lesions by 64-slice computed tomography: a comparative study with quantitative coronary angiography and intravascular ultrasound. *J Am Coll Cardiol* 2005; **46**: 147–54.
- 4) Pugliese F, Mollet NR, Hunink MG, Cademartiri F, Nieman K, van Domburg RT, et al. Diagnostic performance of coronary CT angiography by using different generations of multisection scanners: single-center experience. *Radiology* 2008; **246**: 384–93.
- 5) Pugliese F, Mollet NR, Runza G, van Mieghem C, Meijboom WB, Malagutti P, et al. Diagnostic accuracy of non-invasive 64-slice CT coronary angiography in patients with stable angina pectoris. *Eur Radiol* 2006; **16**: 575–82.
- 6) Schroeder S, Achenbach S, Bengel F, Burgstahler C, Cademartiri F, de Feyter P, et al. Cardiac computed tomography: indications, applications, limitations, and training requirements: report of a Writing Group deployed by the Working Group Nuclear Cardiology and Cardiac CT of the European Society of Cardiology and the European Council of Nuclear Cardiology. *Eur Heart J* 2008; **29**: 531–56.
- 7) Jinzaki M, Sato K, Tanami Y, Yamada M, Kuribayashi S, Anzai T, et al. Novel method of displaying coronary CT angiography. Angiographic view. *Circ J* 2006; **70**: 1661–2.
- 8) Jinzaki M, Sato K, Tanami Y, Yamada M, Anzai T, Kawamura A, et al. Diagnostic accuracy of angiographic view image for the detection of coronary artery stenoses by 64-detector row CT: a pilot study comparison with conventional post-processing methods and axial images alone. *Circ J* 2009; **73**: 691–8.
- 9) Schuijff JD, Wijns W, Jukema JW, Atsma DE, de Roos A, Lamb HJ, et al. Relationship between noninvasive

- coronary angiography with multi-slice computed tomography and myocardial perfusion imaging. *J Am Coll Cardiol* 2006; **48**: 2508–14.
- 10) Pijls NH, van Schaardenburgh P, Manoharan G, Boersma E, Bech JW, van't Veer M, et al. Percutaneous coronary intervention of functionally nonsignificant stenosis; 5-year follow-up of the DEFER study. *J Am Coll Cardiol* 2007; **49**: 2105–11.
 - 11) George RT, Silva C, Cordeiro MA, DiPaula A, Thompson DR, McCarthy WF, et al. Multidetector computed tomography myocardial perfusion imaging during adenosine stress. *J Am Coll Cardiol* 2007; **48**: 153–60.
 - 12) George RT, Silva C, Cordeiro MA, DiPaula A, Thompson DR, McCarthy WF, et al. Quantification of myocardial perfusion using dynamic 64-detector computed tomography. *Invest Radiol* 2007; **42**: 815–22.
 - 13) Rispler S, Keidar Z, Ghersin E, Roguin A, Soil A, Dragu R, et al. Integrated single-photon emission computed tomography and computed tomography coronary angiography for the assessment of hemodynamically significant coronary artery lesions. *J Am Coll Cardiol* 2007; **49**: 1059–67.
 - 14) Gaemperli O, Schepis T, Valenta I, Husmann L, Schefel H, Duerst V, et al. Cardiac image fusion from stand-alone SPECT and CT: clinical experience. *J Nucl Med* 2007; **48**: 696–703.
 - 15) Schroeder S, Kopp AF, Baumbach A, Meisner C, Kuettnner A, Georg C, et al. Noninvasive detection and evaluation of atherosclerotic coronary plaques with multislice computed tomography. *J Am Coll Cardiol* 2001; **37**: 1430–5.
 - 16) Cademartiri F, Mollet NR, Runza G, Bruining N, Hamers R, Somers P, et al. Influence of intracoronary attenuation on coronary plaque measurements using multislice computed tomography: observations in an ex vivo model of coronary computed tomography angiography. *Eur Radiol* 2005; **15**: 1426–31.
 - 17) Motoyama S, Sarai M, Harigaya H, Anno H, Inoue K, Hara T, et al. Computed tomographic angiography characteristics of atherosclerotic plaques subsequently resulting in acute coronary syndrome. *J Am Coll Cardiol* 2009; **54**: 49–57.
 - 18) Leber AW, Becker A, Knez A, von Ziegler F, Sirol M, Nikolaou K, et al. Accuracy of 64-slice computed tomography to classify and quantify plaque volumes in the proximal coronary system: a comparative study using intravascular ultrasound. *J Am Coll Cardiol* 2006; **47**: 672–7.
 - 19) Budoff MJ, Achenbach S, Blumenthal RS, Carr JJ, Goldin JG, Greenland P, et al. Statement from the American Heart Association Committee on Cardiovascular Imaging and Intervention, Council on Cardiovascular Radiology and Intervention, and Committee on Cardiac Imaging, Council on Clinical Cardiology. *Circulation* 2006; **114**: 1761–91.
 - 20) Hendel RC, Patel MR, Kramer CM, Poon M, Hendel RC, Carr JC, et al. ACCF/ACR/SCCT/SCMR/ASNC/NASCI/SCAI/SIR 2006 appropriateness criteria for cardiac computed tomography and cardiac magnetic resonance imaging: a report of the American College of Cardiology Foundation Quality Strategic Directions Committee Appropriateness Criteria Working Group, American College of Radiology, Society of Cardiovascular Computed Tomography, Society for Cardiovascular Magnetic Resonance, American Society of Nuclear Cardiology, North American Society for Cardiac Imaging, Society for Cardiovascular Angiography and Interventions, and Society of Interventional Radiology. *J Am Coll Cardiol* 2006; **48**: 1475–97.
 - 21) Carbonaro S, Villines TC, Hausleiter J, Devine PJ, Gerber TC, Taylor AJ. International, multidisciplinary update of the 2006 appropriateness criteria for cardiac computed tomography. *J Cardiovasc Comput Tomogr* 2009; **3**: 224–32.
 - 22) American College of Cardiology Foundation Task Force on Expert Consensus Documents, Mark DB, Berman DS, Budoff MJ, Carr JJ, Gerber TC, et al. ACCF/ACR/AHA/NASCI/SAIP/SCAI/SCCT 2010 expert consensus document on coronary computed tomographic angiography: a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents. *Circulation* 2010; **121**: 2509–43.
 - 23) ASCI CCT & CMR Guideline Working Group, Tsai IC, Choi BW, Chan C, Jinzaki M, Kitagawa K, et al. ASCI 2010 appropriateness criteria for cardiac computed tomography: a report of the Asian Society of Cardiovascular Imaging cardiac computed tomography and cardiac magnetic resonance imaging guideline Working Group. *Int J Cardiovasc Imaging* 2010; **26** (Suppl 1): 1–15.
 - 24) Abbata S, Arbab-Zadeh A, Callister TQ, Desai MY, Mamuya W, Thomson L, et al. SCCT guidelines for performance of coronary computed tomographic angiography: A report of the Society of Cardiovascular Computed Tomography Guidelines Committee. *J Cardiovasc Comput Tomogr* 2009; **3**: 190–204.
 - 25) Raff GL, Abidov A, Achenbach S, Berman DS, Bort LM, Budoff MJ, et al. SCCT guidelines for the interpretation and reporting of coronary computed tomographic angiography. *J Cardiovasc Comput Tomogr* 2009; **3**: 122–36.
 - 26) 2007–2008 joint study group report. Guidelines for diagnosis and treatment of circulatory diseases: Guidelines for noninvasive diagnosis of coronary arterial lesions. *Circ J* 2009; **73** (Suppl III): 1019–89.
 - 27) Nakazawa G, Tanabe K, Onuma Y, Yachi S, Aoki J, Yamamoto H, et al. Efficacy of culprit plaque assessment by 64-slice multidetector computed tomography to predict transient no-reflow phenomenon during percutaneous coronary intervention. *Am Heart J* 2008; **155**: 1150–7.
 - 28) Soon KH, Selvanayagam JB, Cox N, Kelly AM, Bell KW, Lim YL. Percutaneous revascularization of chronic total occlusions: review of the role of invasive and non-invasive imaging modalities. *Int J Cardiol*

- 2007; **116**: 1–6.
- 29) Hoffmann U, Nagurney JT, Moselewski F, Pena A, Ferencik M, Chae CU, et al. Coronary multidetector computed tomography in the assessment of patients with acute chest pain. *Circulation* 2006; **114**: 2251–60.
- 30) Gallagher MJ, Ross MA, Raff GL, Goldstein JA, O'Neill WW, O'Neil B, et al. The diagnostic accuracy of 64-slice computed tomography coronary angiography compared with stress nuclear imaging in emergency department low-risk chest pain patients. *Ann Emerg Med* 2007; **49**: 125–36.
- 31) Rubinshtein R, Halon DA, Gaspar T, Jaffe R, Karkabi B, Flugelman MY, et al. Usefulness of 64-slice cardiac computed tomographic angiography for diagnosing acute coronary syndromes and predicting clinical outcome in emergency department patients with chest pain of uncertain origin. *Circulation* 2007; **115**: 1762–8.
- 32) Meijboom WB, Mollet NR, Van Mieghem CA, Weustink AC, Pugliese F, van Pelt N, et al. 64-slice CT coronary angiography in patients with non-ST elevation acute coronary syndrome. *Heart* 2007; **93**: 1386–92.
- 33) Ueno K, Anzai T, Jinzaki M, Yamada M, Kohnō T, Kawamura A, et al. Diagnostic capacity of 64-slice multidetector computed tomography for acute coronary syndrome in patients presenting with acute chest pain. *Cardiology* 2009; **112**: 211–8.
- 34) Rixe J, Achenbach S, Ropers D, Baum U, Kuettner A, Ropers U, et al. Assessment of coronary artery stent restenosis by 64-slice multi-detector computed tomography. *Eur Heart J* 2006; **27**: 2567–72.
- 35) Jones CM, Athanasiou T, Dunne N, Kirby J, Aziz O, Haq A, et al. Multi-detector computed tomography in coronary artery bypass graft assessment: a meta-analysis. *Ann Thorac Surg* 2007; **83**: 341–8.
- 36) Hamon M, Lepage O, Malagutti P, Riddell JW, Morello R, Agostini D, et al. Diagnostic performance of 16- and 64-section spiral CT for coronary artery bypass graft assessment: meta-analysis. *Radiology* 2008; **247**: 679–86.
- 37) Ropers D, Pohle FK, Kuettner A, Pflederer T, Anders K, Daniel WG, et al. Diagnostic accuracy of noninvasive coronary angiography in patients after bypass surgery using 64-slice spiral computed tomography with 330-ms gantry rotation. *Circulation* 2006; **114**: 2334–41.
- 38) Bluemke DA, Achenbach S, Budoff M, Gerber TC, Gersh B, Hillis LD, et al. Noninvasive coronary artery imaging: magnetic resonance angiography and multidetector computed tomography angiography: a scientific statement from the American heart association committee on cardiovascular imaging and intervention of the council on cardiovascular radiology and intervention, and the councils on clinical cardiology and cardiovascular disease in the young. *Circulation* 2008; **118**: 586–606.
- 39) Jakobs TF, Becker CR, Ohnesorge B, Flohr T, Suess C, Schoepf UJ, et al. Multislice helical CT of the heart with retrospective ECG gating: reduction of radiation exposure by ECG-controlled tube current modulation. *Eur Radiol* 2002; **12**: 1081–6.
- 40) Hirai N, Horiguchi J, Fujioka C, Kiguchi M, Yamamoto H, Matsuura N, et al. Prospective versus retrospective ECG-gated 64-detector coronary CT angiography: assessment of image quality, stenosis, and radiation dose. *Radiology* 2008; **248**: 424–30.
- 41) Leipsic J, Labounty TM, Heilbron B, Min JK, Mancini GBJ, Lin FY, et al. Estimated radiation dose reduction using adaptive statistical iterative reconstruction in coronary CT angiography: the ERASIR study. *AJR Am J Roentgenol* 2010; **195**: 655–60.
- 42) Yamada M, Jinzaki M, Imai Y, Yamazaki S, Imanishi N, Tanami Y, et al. Evaluation of severely calcified coronary artery using fast-switching dual-kVp 64-slice computed tomography. *Circ J* 2011; **75**: 472–3.

➤ Review Article ◀

Prophylactic Implantation of Inferior Vena Cava Filter during Endovascular Therapies for Deep Venous Thrombosis of the Lower Extremities

Takuji Yamagami, MD, PhD and Tsunehiko Nishimura, MD, PhD

Patients with deep venous thrombosis (DVT) of the lower extremities have an increased risk of pulmonary emboli and post-thrombotic syndrome. Traditionally, they are treated medicinally, with anticoagulation therapy. Currently, endovascular therapies, with their higher efficiency, have replaced previously attempted systemic fibrinolytic therapies. There is a continuing controversy in the temporary use of filters in the inferior vena cava during these endovascular therapies, which may include catheter-directed thrombolysis, manual aspiration, mechanical thrombectomy, percutaneous transluminal angioplasty and placement of self-expandable metallic stents. Here, we present an overview of the literature and analysis on the application of prophylactic implantation of an inferior vena cava filter during endovascular therapy for DVT of the lower extremities.

Key words: embolism, pulmonary, endovascular therapies, extremities, thrombosis, vena cava, filters

INTRODUCTION

The initial symptoms of deep venous thrombosis (DVT) in the lower extremities may be quite severe,^{1,2)} and, additionally, there is a substantial risk of pulmonary embolism in patients with DVT.^{1,3)} Moreover, when DVTs remain, there is the possibility of delayed complications, including the spectrum of debilitating symptoms referred to as post-thrombotic syndrome.⁴⁾ Therefore, treatment of DVT is necessary. Traditionally, therapy for DVT has consisted in systemic IV administration of heparin.⁵⁾ Other options have been systemic IV administration of fibrinolytic agents such as urokinase or streptokinase.⁵⁻⁷⁾ Recombinant tissue plasminogen activator has gained attention as an effective fibrinolytic agent.^{8,9)} Systemic

thrombolysis is more effective than heparinization but less effective than catheter-directed thrombolysis. Catheter-directed thrombolysis, an endovascular therapy, has become a widely accepted treatment for DVT.^{4,9-11)} For improving the quality of treatment for DVT, other endovascular procedures: manual aspiration of the thrombus,¹²⁾ mechanical thrombectomy,^{4,13,14)} percutaneous transluminal angioplasty^{13,15)} and self-expandable metallic stent placement^{4,13,15,16)} are sometimes used in combination with catheter-directed thrombolysis.

Theoretically, a thrombus released from the DVT during catheter-directed thrombolysis could move to the pulmonary artery, resulting in pulmonary thromboembolism. DVT and pulmonary thromboembolism comprise venous thromboembolism (VTE). Then, implantation of inferior vena cava filters has been applied prophylactically to prevent such an occurrence.¹⁷⁻²⁰⁾ However, this is considered to be unnecessary by some,^{1,10,11)} with the result that this procedure is very controversial.^{1,9-11,17-21)} This article presents an overview of the literature regarding the application of prophylactic implantation of an inferior vena cava filter during endovascular therapy for DVT of the lower extremities. We also present our conclusions drawn through examination of the literature on this topic.

Department of Radiology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Kyoto, Japan

Received: September 9, 2010; Accepted: December 14, 2010
Corresponding author: Takuji Yamagami, MD, PhD. Department of Radiology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, 465 Kajii-cho, Kawaramachi-Hirokoji, Kamigyo-ku, Kyoto, Kyoto 602-8566, Japan
Tel: +81-75-251-5620, Fax: +81-75-251-5840
E-mail: yamagami@koto.kpu-m.ac.jp

TYPE OF FILTERS

There are 3 types of filters: permanent, temporary or optional. When only short-term protection is required, ideally, a permanent inferior vena cava filter would not be placed, particularly if a long life is expected for the patient, considering the demerits of permanent filter implantation with high frequency of recurrence of DVT.²²⁾ Thus, a temporary vena cava filter has been widely used for this purpose.^{23, 24)} However, paralleling the increased use of temporary vena cava filters, complications have been described that were mainly associated with their structure, in that part of the device projects from the insertion site.²⁴⁻²⁶⁾ Some of these complications were serious, and included infection where the device protruded from the insertion site,²⁷⁾ air embolism through a defective sheath,²⁴⁾ worsening of proximal thrombosis along the attached catheter,²⁵⁾ and migration of the filter into the pulmonary artery.²⁶⁾ Moreover, temporary filters must be replaced by permanent filters²⁴⁾ when the maximal implantation period is reached before successful completion of therapy for DVT. Because of the above-mentioned complications and problems with temporary vena cava filters, the use of an optional vena cava filter that could be implanted without an attached catheter or guide-wire would be advantageous. If necessary, this filter could also serve as a permanent filter.^{28, 29)}

PROPHYLACTIC USE OF AN INFERIOR VENA CAVA FILTER DURING ENDOVASCULAR THERAPIES FOR DEEP VENOUS THROMBOSIS

The use of filters in the inferior vena cava temporarily during endovascular therapies for DVT of the lower extremities remains controversial.

Placement of an inferior vena cava filter during catheter-directed thrombolysis has been proposed as necessary in patients who have large, mobile, free-floating thrombi within the inferior vena cava.¹⁾ Some investigators,⁹⁻¹¹⁾ insist that the prophylactic use of an inferior vena cava filter during catheter-directed thrombolysis is unnecessary because of the low rate of pulmonary embolism. For these patients, the viewpoint is supported by Bjarnason et al.¹⁾ who reported only 2 (0.9%) of 214 patients developing pulmonary embolism, and by Mewissen et al.¹¹⁾ who reported only 6 (1.3%) of 473 patients; however, 1 of these was a fatality.

On the other hand, support of the use of temporary vena cava filters can be found in the literature. In a summary

of their experience with implantation of temporary vena cava filters in 132 patients with DVT who were receiving thrombolytic therapy, Thery et al.³⁰⁾ had observed lysing of a clot by thrombolytic therapy in the filter in 41 (31%) of 132 patients. Since none of the 132 patients experienced pulmonary embolism, they suggested that the filter might have prevented the pulmonary embolism during thrombolytic treatment in at least 41 of the patients. It has been proposed^{17-21, 27, 31, 32)} that the prophylactic use of an inferior vena cava filter is necessary, in view of the high rate of trapping a thrombus in these filters during therapies for DVT as revealed by Thery et al.³⁰⁾ and great importance has been attached to its potential in reducing mortality, though the rate is low.¹¹⁾

In situations that limit the dosage of anticoagulation or fibrinolytic agents, for example, in patients with traumatic injury or after surgery, another endovascular therapy should completely replace or should be added to catheter-directed thrombolysis. In some countries, dosage of such drugs is very limited compared with that in western countries. In Japan, for example, dosages of drugs administered for catheter-directed thrombolysis are kept within the dosage permitted by the Japanese government-subsidized health insurance programs and the usage of certain drugs is not permitted. In those programs, use of urokinase is limited to 240000 IU per day and tissue plasminogen activator variants are not permitted, in principle, for therapy of deep venous thrombosis.²¹⁾ Because of this situation, the effectiveness of catheter-directed thrombolysis must be inferior to that in circumstances in which anticoagulation or fibrinolytic agents can be used in large quantities, as in western countries. Thus, other endovascular therapies such as manual aspiration of thrombus and mechanical thrombectomy must be added in many cases. However, there has been little discussion on the necessity of filter placement during therapies for DVT with interventional radiological procedures other than catheter-directed thrombolysis.²¹⁾

In one study of patients on therapies for DVT including systematic anticoagulation therapy in Japan, a clot of trapped thrombus was observed in 83% of 30 retrieved filters that had been implanted optionally during therapy for DVT.³²⁾ When an optional inferior vena cava filter was implanted prophylactically during endovascular therapies for DVT in 17 patients, pulmonary embolism was avoided in all; however, in 47.1% (n = 8), a trapped thrombus was observed in the filter on venography performed during endovascular therapies.²⁸⁾ Results of prophylactic implantation of an inferior vena cava filter dur-

ing endovascular therapies for DVT of the lower extremity with a larger number of subjects showed that in 20 (54.1%) of 37 endovascular therapy sessions and in 22 of 66 filters implanted, a trapped clot of thrombus was observed on venography.²⁹ The trapped thrombus filled <1/4 the height of the filter in 2, from $\geq 1/4$ to <1/2 in 6, and $\geq 1/2$ but within the height of the filter in 7. In the remaining 7 of 22 filters, the trapped thrombus occupied greater than the height of the filter. It is possible that if the filters had not been implanted, the thrombus might have moved to the pulmonary artery, causing pulmonary embolism. There is special concern when the captured thrombus is larger than half the height of the filter.

CHALLENGES IN FILTER RETRIEVAL WHEN A LARGE THROMBUS IS TRAPPED IN THE FILTER

The presence of a large thrombus in a filter at the time of filter removal can be problematic.³³⁻³⁵ Removal of the Gunther tulip vena cava filter (Cook, Bjaeverskov, Denmark), which is one of the optional vena cava filters, is contraindicated by the manufacturer when the thrombus fills more than 1/4 of the filter cone.³³ Also, in the retrieval of the OptEase filter, another optional vena cava filter, Oliva et al.³⁵ recommended not to attempt filter retrieval if the trapped thrombus is larger than 5 mm in width and/or 20 mm in length. However, in practice, as mentioned above, in certain situations, it is more favorable to remove the filter. Thus, modifying the usual methods for removal of the filter would be helpful in achieving a successful removal. In retrieval of the Gunther tulip vena cava filter, Kinney³⁴ suggested that fibrinolytic therapy could be used to reduce or remove the entrapped clot in preparation for filter removal. In the study of Yamagami et al.,²⁹ in 20 filters, the captured thrombus filled more than 1/4 the height of the filter. For these cases, they used a combination of catheter-directed thrombolysis, manual aspiration, and temporary filtering by temporarily positioning another filter at the cephalad side of the filter with the trapped clot to remove the filter safely. During removal of these filters, the pulmonary embolism did not develop or get worse.

VENOUS THROMBOEMBOLISM AFTER RETRIEVAL OF OPTIONAL VENA CAVA FILTERS

In addition to reports evaluating the retrievability of optional vena cava filters,^{27,28,35,36} a follow-up of patients after retrieval with regard to recurrent DVT following

removal has been reported.^{27,37,38} In a report by Millward et al.²⁷ describing a mean follow-up of 103 days, DVT recurred in 1 (2.7%) of 37 patients in whom the filter was removed. Asch et al.³⁷ reported that 1 (4.5%) pulmonary embolism occurred among 22 patients during a post-retrieval clinical follow-up of an average of 223 days with Recovery filters. In a follow-up period of 20.6 months, after retrieval of 72 filters implanted in 67 patients, Yavuz et al.³⁸ observed a recurrent DVT in 2 of the 67 patients. Yamagami et al.³⁹ described the observation of 76 patients after retrieval of optional filters; the rate of recurrent pulmonary embolism was 2.0% and that of DVT was 4.6%. The incidence of recurrent VTE in one study³⁹ was similar to what was reported in other studies, although the follow-up period was much longer and the number of patients was larger.^{27,37,38} In that series,³⁹ the mean follow-up period after retrieval of the filter was 39.8 ± 22.1 months (range, 6–84 months). Such favorable results might have been obtained because the outpatient care was adequate and long-term, and included monitoring the condition of patients with ultrasound, enhanced CT and blood tests such as D-dimer assays. In that series, risk factors for recurrent VTE after filter removal were also investigated.³⁹ There was a tendency for recurrence of VTE at a higher rate in cases in whom the status of DVT before filter implantation was so severe that endovascular therapies for DVT were required and in whom DVT remained at the time of filter removal. However, the difference between those with and without these risk factors was not statistically significant.

CONCLUSION

In reviewing previous reports,^{28-30,32} we want to reiterate that, despite the strong controversy as to whether to use filters temporarily in the inferior vena cava during endovascular therapies for deep venous thrombosis, the inferior vena cava filter played an important role in filtering a thrombus released from the lower limb, thereby preventing pulmonary embolism. Thus, use of the optional vena cava filter is recommended during endovascular therapies for deep venous thrombosis. However, long-term follow up to avoid recurrence of venous thromboembolism after retrieval of the filter is necessary.

REFERENCES

- 1) Bjarnason H, Kruse JR, Asinger DA, Nazarian GK, Dietz CA Jr, Caldwell MD, et al. Iliofemoral deep

- venous thrombosis: safety and efficacy outcome during 5 years of catheter-directed thrombolytic therapy. *J Vasc Interv Radiol* 1997; **8**: 405–18.
- 2) Strandness DE Jr, Langlois Y, Cramer M, Randlett A, Thiele BL. Long-term sequelae of acute venous thrombosis. *JAMA* 1983; **250**: 1289–92.
- 3) Hirsch J, Hoak J. Management of deep vein thrombosis and pulmonary embolism. *Circulation* 1996; **93**: 2212–45.
- 4) Sharafuddin MJ, Sun S, Hoballah JJ, Youness FM, Sharp WJ, Roh BS. Endovascular management of venous thrombotic and occlusive diseases of the lower extremities. *J Vasc Interv Radiol* 2003; **14**: 405–23.
- 5) Elliot MS, Immelman EJ, Jeffery P, Benatar SR, Funston MR, Smith JA, et al. A comparative randomized trial of heparin versus streptokinase in the treatment of acute proximal venous thrombosis: an interim report of a prospective trial. *Br J Surg* 1979; **66**: 838–43.
- 6) Arnesen H, Hoiseth A, Ly B. Streptokinase or heparin in the treatment of deep vein thrombosis. *Acta Med Scand* 1982; **211**: 65–8.
- 7) Robertson BR, Nilsson JM, Nylander G. Value of streptokinase and heparin in treatment of acute deep venous thrombosis. *Acta Chir Scand* 1968; **134**: 203–8.
- 8) Sugimoto K, Hofmann LV, Razavi MK, Kee ST, Sze DY, Dake MD, et al. The safety, efficacy, and pharmacoeconomics of low-dose alteplase compared with urokinase for catheter-directed thrombolysis of arterial and venous occlusions. *J Vasc Surg* 2003; **37**: 512–7.
- 9) Grossman C, McPherson S. Safety and efficacy of catheter-directed thrombolysis for iliofemoral venous thrombosis. *AJR* 1998; **172**: 667–72.
- 10) Semba CP, Dake MD. Iliofemoral deep venous thrombosis: Aggressive therapy with catheter-directed thrombolysis. *Radiology* 1994; **191**: 487–94.
- 11) Mewissen MW, Seabrook GR, Meissner MH, Cynamon J, Labropoulos N, Haughton SH. Catheter-directed thrombolysis for lower extremity deep venous thrombosis: report of a national multicenter registry. *Radiology* 1999; **211**: 39–49.
- 12) Roy S, Laerum F. Transcatheter aspiration: The key to successful percutaneous treatment of deep venous thrombosis? *Acad Radiol* 1999; **6**: 730–5.
- 13) Bravo SM, Reinhart RD, Meyerovitz MF. Percutaneous venous interventions. *Vasc Med* 1998; **3**: 61–6.
- 14) Delomez M, Beregi JP, Willoteaux S, Bauchart JJ, d’Othee BJ, Asseman P, et al. Mechanical thrombectomy in patients with deep venous thrombosis. *Cardiovasc Interv Radiol* 2001; **24**: 42–8.
- 15) AbuRahma AF, Perkins SE, Wulu JT, Ng HK. Iliofemoral deep vein thrombosis: conventional therapy versus lysis and percutaneous transluminal angioplasty and stenting. *Ann Surg* 2001; **233**: 752–60.
- 16) Nazarian GK, Bjarnason H, Dietz CA Jr, Bernadas CA, Hunter DW. Iliofemoral venous stenoses: effectiveness of treatment with metallic endovascular stents. *Radiology* 1996; **200**: 193–9.
- 17) Neuerburg J, Günther RW. Developments in inferior vena cava filters: a European viewpoint. *Semin Interv Radiol* 1994; **11**: 349–57.
- 18) Millward S. Temporary and retrievable inferior vena cava filters: current status. *J Vasc Interv Radiol* 1998; **9**: 381–7.
- 19) Emanuelli G, Segrà V, Frigerio C. Selected strategies in venous thromboembolism: local thrombolytic treatment and caval filters. *Haematologica* 1995; **80**: 84–6.
- 20) Palombo D, Porta C, Brustia P, Peinetti F, Udini M, Antico A, et al. Loco-regional thrombolysis in deep venous thrombosis. *Phlebologie* 1993; **46**: 293–302.
- 21) Yamagami T, Kato T, Iida S, Tanaka O, Nishimura T. Retrievable vena cava filter placement during treatment for deep venous thrombosis. *Br J Radiol* 2003; **76**: 712–8.
- 22) Decousus H, Leizorovicz A, Parent F, Page Y, Tardy B, Girard P, et al. A clinical trial of vena caval filters in the prevention of pulmonary embolism in patients with proximal deep-vein thrombosis. *N Engl J Med* 1998; **338**: 409–15.
- 23) Neuerburg J, Günther RW. Developments in inferior vena cava filters: a European viewpoint. *Semin Interv Radiol* 1994; **11**: 349–57.
- 24) Lorch H, Welger D, Wagner V, Hillner B, Strecker EP, Herrmann H, et al. Current practice of temporary vena cava filter insertion: a multicenter registry. *J Vasc Interv Radiol* 2000; **11**: 83–8.
- 25) Carcone B, Pernes JM, Carcopino JM, Chollet D, Pouillard F. Worsening of proximal thrombosis after insertion of a temporary caval filter (3 cases). *Rev Med Interne* 1995; **16**: 351–3.
- 26) Stosslein F, Altmann E. A rare complication with an Antheor vena cava filter. *Cardiovasc Interv Radiol* 1998; **21**: 165–7.
- 27) Millward SF, Oliva VL, Bell SD, Valenti DA, Rasuli P, Asch M, et al. Gunther tulip retrievable vena cava filter: results from the registry of the Canadian interventional radiology association. *J Vasc Interv Radiol* 2001; **12**: 1053–8.
- 28) Yamagami T, Kato T, Hirota T, Yoshimatsu R, Matsumoto T, Nishimura T. Prophylactic implantation of inferior vena cava filter during interventional radiological treatment for deep venous thrombosis of the lower extremity. *Br J Radiol* 2006; **79**: 584–91.
- 29) Yamagami T, Yoshimatsu R, Matsumoto T, Nishimura T. Prophylactic implantation of inferior vena cava filter during endovascular therapies for deep venous thrombosis of the lower extremity: is it necessary? *Acta Radiol* 2008; **49**: 391–7.
- 30) Thery C, Bauchart JJ, Lesenne M, Asseman P, Flajollet JG, Legghe R, et al. Predictive factors of effectiveness of streptokinase in deep venous thrombosis. *Am J Cardiol* 1992; **69**: 117–22.
- 31) Millward SF, Bhargava A, Aquino J Jr, Peterson RA, Veinot JP, Bormanis J, et al. Gunther tulip filter: preliminary clinical experience with retrieval. *J Vasc Interv Radiol* 2000; **11**: 75–82.
- 32) Yamagami T, Kato T, Iida S, Hirota T, Nishimura T.

- Gunther tulip inferior vena cava filter placement during treatment for deep venous thrombosis of the lower extremity. *Cardiovasc Intervent Radiol* 2005; **28**: 442–53.
- 33) Kerlan RK Jr, LaBerge JM, Wilson MW, Gordon RL. Residual thrombus within a retrievable IVC filter. *J Vasc Interv Radiol* 2005; **16**: 555–7.
 - 34) Kinney TB. Update on inferior vena cava filters. *J Vasc Interv Radiol* 2003; **14**: 425–40.
 - 35) Oliva VL, Szatmari F, Giroux MF, Klemming BK, Cohen SA, Soulez G. The Jonas study: evaluation of the retrievability of the Cordis OptEase inferior vena cava filter. *J Vasc Interv Radiol* 2005; **16**: 1439–45.
 - 36) Yamagami T, Kato T, Hirota T, Yoshimatsu R, Matsumoto T, Nishimura T. Evaluation of retrievability of the Gunther tulip vena cava filter. *Cardiovasc Intervent Radiol* 2007; **30**: 226–31.
 - 37) Asch MR. Initial experience in humans with a new retrievable inferior vena cava filter. *Radiology* 2002; **225**: 835–44.
 - 38) Yavuz K, Geyik S, Hoppe H, Kolbeck KJ, Kaufman JA. Venous thromboembolism after retrieval of inferior vena cava filters. *J Vasc Interv Radiol* 2008; **19**: 504–8.
 - 39) Yamagami T, Tanaka O, Yoshimatsu R, Miura H, nishimura T. Venous thromboembolism after removal of retrievable inferior vena cava filters. *Cardiovasc Intervent Radiol* 2010; **33**: 74–9.

Original Article

Prediction of Limb Salvage after Therapeutic Angiogenesis by Autologous Bone Marrow Cell Implantation in Patients with Critical Limb Ischemia

Shuhei Tara, MD, PhD,¹ Masaaki Miyamoto, MD, FACS,¹ Gen Takagi, MD, PhD,¹
Yoshimitsu Fukushima, MD, PhD,² Sonoko Kirinoki-Ichikawa, MD,¹ Hitoshi Takano, MD, PhD,¹
Ikuyo Takagi, MD, PhD,¹ Hiroshi Mizuno, MD, PhD,³ Masahiro Yasutake, MD, PhD,¹
Shinichiro Kumita, MD, PhD,² and Kyoichi Mizuno MD, PhD¹

Purpose: Despite advances in therapeutic angiogenesis by bone marrow cell implantation (BMCI), limb amputation remains a major unfavorable outcome in patients with critical limb ischemia (CLI). We sought to identify predictor(s) of limb salvage in CLI patients who received BMCI.

Materials and Methods: Nineteen patients with CLI who treated by BMCI were divided into two groups; four patients with above-the-ankle amputation by 12 weeks after BMCI (amputation group) and the remaining 15 patients without (salvage group). We performed several blood-flow examinations before BMCI. Ankle-brachial index (ABI) was measured with the standard method. Transcutaneous oxygen tension (TcPO₂) was measured at the dorsum of the foot, in the absence (baseline) and presence (maximum TcPO₂) of oxygen inhalation. ^{99m}technetium-tetrofosmin (^{99m}Tc-TF) perfusion index was determined at the foot and lower leg as the ratio of brain.

Results: Maximum TcPO₂ ($p = 0.031$) and ^{99m}Tc-TF perfusion index in the foot ($p = 0.0068$) was significantly higher in the salvage group than in the amputation group. Receiver operating characteristic (ROC) curve analysis identified maximum TcPO₂ and ^{99m}Tc-TF perfusion index in the foot as having high predictive accuracy for limb salvage.

Conclusion: Maximum TcPO₂ and ^{99m}Tc-TF perfusion index in the foot are promising predictors of limb salvage after BMCI in CLI.

Key words: critical limb ischemia, bone marrow cell implantation, limb salvage, ^{99m}technetium-tetrofosmin perfusion scintigraphy, transcutaneous oxygen tension

¹Division of Cardiology, Department of Internal Medicine, Nippon Medical School, Tokyo, Japan

²Department of Radiology, Nippon Medical School, Tokyo, Japan

³Department of Plastic and Reconstructive Surgery, Nippon Medical School, Tokyo, Japan

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Corresponding author: Masaaki Miyamoto, MD, FACS. Division of Cardiology, Department of Internal Medicine, Nippon Medical School, 1-1-5, Sendagi, Bunkyo-ku, Tokyo 113-8603, Japan
Tel: +81-3-3822-2131 (ext. 6743), Fax: +81-3-5685-0987
E-mail: miyamoto-m@nms.ac.jp

INTRODUCTION

Peripheral arterial disease (PAD) is a progressive illness primarily due to atherosclerosis. It also occurs in Buerger's disease and collagen disease involving vasculitis in small and medium-sized arteries. The most severe manifestation is termed "critical limb ischemia (CLI)," as demonstrated by ischemic rest pain and/or loss of tissue integrity, including skin ulceration and gangrene.¹⁾ PAD relates to a worse long-term outcome²⁾; furthermore, only 45% of CLI patients were free from limb amputation or

death within a year after diagnosis.¹⁾ The current goals of management of CLI are to relieve ischemic pain, heal ischemic ulcers, and prevent major limb amputation, in addition to reducing cardiovascular mortality.

Recent advances in surgical and percutaneous revascularization have led to better treatment options for patients with CLI.³⁾ Notably, revascularization is not suitable in a considerable proportion of patients (10–15%) (“no-option patients”). Of these patients, more than 40% would require a major limb amputation, and 20% would die within 6 months.⁴⁾ For such “no-option patients,” therapeutic angiogenesis by autologous bone marrow cell implantation (BMCI) has emerged as a novel strategy in an attempt to improve blood perfusion at the ischemic site, and evidence has accumulated that BMCI is a safe and effective treatment for CLI.^{5,6)}

Because the clinical condition of patients with CLI changes with time, repeated blood flow examinations are necessary. Thus, it is important to establish non-invasive and convenient examinations to detect blood flow. The ankle-brachial index (ABI) is convenient and the most utilized method to diagnose PAD, and transcutaneous oxygen tension (TcPO₂) is one of the commonly used noninvasive examinations reflecting local arterial blood flow.^{7,8)} Amann et al. reported that TcPO₂ is a useful measurement for evaluating blood flow recovery in patients with CLI who underwent BMCI.⁹⁾ In a previous investigation, we demonstrated that ^{99m}technetium-tetrofosmin (^{99m}Tc-TF) perfusion scintigraphy is useful for the assessment of quantitative blood flow after BMCI.⁵⁾ However, among these non-invasive examinations of blood flow, predictors of limb salvage in patients with CLI subjected to BMCI have not been established.

The aim of this study was to evaluate the usefulness of these non-invasive measurements of blood flow as predictors of limb salvage after BMCI in patients with CLI.

METHODS

Patient selection

We enrolled 20 consecutive patients who gave their written informed consent and who met the following criteria: a) atherosclerotic PAD or Buerger's disease with total occlusion or severe stenosis of leg arteries below popliteal artery diagnosed by digital subtraction angiography, b) CLI with Rutherford classification II-4 to IV-6 (Fontaine class 3 or 4) unsuitable for peripheral catheter intervention or bypass surgery, c) continuous ischemic symptoms for more than 6 months despite other conven-

tional treatments, d) no evidence of malignant disorder during the past 5 years and no proliferative diabetic retinopathy, e) male or female aged 20–79 years. Preoperative screening was performed as described previously,⁵⁾ and the therapeutic decision was made by the advisory committee (consisting of cardiologists, vascular surgeons, plastic surgeons, radiologists and anesthesiologists).

At 12 weeks of follow up after BMCI, the patients were retrospectively divided into a salvage group (n = 15) and an amputation group (n = 4). Major amputation was defined as amputation above the ankle joint,³⁾ and limb salvage was defined as avoidance of major amputation. We performed partial amputation of the toes for complete necrosis or local osteomyelitis. One patient was excluded from this study because he died of congestive heart failure 60 days after BMCI.

The medical ethics committee of Nippon Medical School reviewed and approved this clinical trial.

Cell preparation and implantation

Bone marrow cell implantation was performed as described previously.⁵⁾ In brief, approximately 500 ml of bone marrow fluid was aspirated from the bilateral iliac bones of the patient under general anesthesia and collected in a sterile bag containing heparinized (20,000 units) RPMI 1640 medium (GIBCO, Grand Island, NY). The mononuclear cell fraction was sorted using an AS TEC 204 blood cell separator (Fresenius Kabi, Bad Homburg, Germany) and processed to obtain a final volume of about 70 ml. Finally, we injected the mononuclear cell suspension (1 ml/point) intramuscularly into the ischemic regions.

Assessment of limb ischemia

ABI was determined as the ratio of ankle systolic blood pressure to brachial systolic blood pressure, with both measured using an automatic device (PWV / ABI; Colin, Ltd., Komaki, Japan). The device simultaneously measured bilateral brachial and ankle blood pressure by the modified oscillometric pressure sensor method. The higher brachial pressure on either the left or right was used for calculating ABI. It was not possible to assess ABI in one patient in the salvage group because of cuff pain.

TcPO₂ was measured by a TCM 400 (RADIOMETER Inc., Tokyo, Japan). The sampling site was carefully selected so as not to overlie a bony prominence, superficial vessel, or pulse site. After wiping the skin with alcohol, we placed a transducer on the dorsum of the ischemic limb and warmed the skin to 43.5 °C to increase the

permeability of the skin to oxygen molecules at the measurement site. With the patient resting in the supine position, we acquired baseline TcPO₂ at ambient conditions for about 20 min. Then, we repeated the acquisition, this time at 5 L/min pure oxygen inhalation for 5 min, to determine the TcPO₂ value in response to an oxygen challenge (maximum TcPO₂).

^{99m}Tc-TF perfusion scintigraphy was performed as described previously.¹⁰⁾ Simply, approximately 10 min after intravenous injection of ^{99m}Tc-TF (555–740 MBq), we performed whole-body scintigraphy of the patient in the prone position, for both anterior and posterior projections, with a dual-head large field-of-view gamma camera (Vertex, ADAC). Each head of the gamma camera was equipped with a high-resolution, low-energy collimator. Scan speed was 12 cm/min. Image acquisition time was approximately 15 min. Data were acquired in a 512 × 1024 matrix and a 2096 window centered on the 140 keV photopeak of ^{99m}Tc. Both the anterior and posterior views were used for the quantitative analysis. Regions of interest (ROI) of equal size were drawn around the lower leg (region from knee to ankle) and the foot (region from ankle to toes) in the anterior and posterior projections (muscle uptake; M).¹⁰⁾ Additionally, intracranial uptake (brain uptake; B) was obtained and used as background. ^{99m}Tc-TF perfusion index was defined as muscle-to-brain (M/B) ratio of averaged counts per pixel.⁵⁾ Two patients in the salvage group did not undergo ^{99m}Tc-TF perfusion scintigraphy.

Statistical analysis

All data are presented as mean ± SD. Intergroup comparisons were made with Student's t test or chi-squared test. Receiver operating characteristic (ROC) curves were constructed to evaluate the predictive accuracy of examinations. Areas under the ROC curves and their 95% confidence intervals (CI) were calculated and compared using a nonparametric test. Then, the best cut-off value for each measurement to predict limb salvage was determined as the one that minimized the distance to the ideal point (sensitivity = specificity = 1) on the ROC curve.¹¹⁾ Time to major limb amputation was compared between the two groups, divided by the cut-off value using Kaplan-Meier analysis with the log-rank test. A value of $p < 0.05$ was considered to be statistically significant.

RESULTS

Clinical characteristics

The overall limb salvage rate in this study was 79%. The reasons for major amputation were uncontrolled infection ($n = 3$) and acute limb ischemia ($n = 1$). The clinical characteristics of the limb salvage and amputation groups are summarized in **Table 1**. The major cause of CLI was atherosclerotic PAD, but five patients with Buerger's disease were included in the salvage group. There was no significant difference between the two groups in age, sex, Rutherford classification (Fontaine class), prevalence of smoking, hypertension, diabetes and hemodialysis. The use of aspirin, cilostazol, anti-hypertensive drugs, statins and insulin did not significantly differ between the two groups. Laboratory data before BMCI were also comparable between the two groups; however, LDL-cholesterol and estimated GFR were significantly higher in the salvage group than in the amputation group ($p < 0.05$). The number of collected bone marrow mononuclear cells was $6.0 \pm 3.5 \times 10^9$ in the salvage group and $4.9 \pm 1.1 \times 10^9$ in the amputation group, with no significant difference between the two groups.

Perfusion parameters prior to BMCI

Fig. 1 shows ABI within one week before BMCI. There was no significant difference in ABI between the two groups (0.71 ± 0.34 in salvage group vs. 0.59 ± 0.63 in amputation group, $p = 0.59$). In **Fig. 2**, TcPO₂ values in the absence (baseline) or presence (maximum) of pure oxygen inhalation were compared. Although the difference in baseline TcPO₂ between the two groups was not significant (25 ± 14 vs. 13 ± 15 mmHg, $p = 0.14$) (**Fig. 2A**), maximum TcPO₂ was significantly higher in the salvage group than in the amputation group (42 ± 24 vs. 12 ± 14 mmHg, $p < 0.05$) (**Fig. 2B**). **Fig. 3** shows a representative image of ^{99m}Tc-TF perfusion scintigraphy, and perfusion index at the foot (ankle to toes), and lower leg (knee to ankle) regions were calculated. The perfusion index in the lower leg region was comparable between the two groups (0.98 ± 0.16 vs. 0.98 ± 0.10 , $p = 0.94$) (**Fig. 4A**). In contrast, tissue perfusion of the foot region was estimated to be significantly greater in the salvage group than in the amputation group (0.84 ± 0.25 vs. 0.42 ± 0.14 , $p = 0.0068$) (**Fig. 4B**).

Cut-off values for limb salvage

The area under the ROC curve was 0.85 [95% CI 0.66–1.05; $p = 0.036$] for maximum TcPO₂ and 0.94 [95%

Table 1 Clinical characteristics

	Limb Salvage group (n = 15)	Major Amputation group (n = 4)	p value
Age (years)	57 ± 14	68 ± 8.3	0.17
Male / Female (%)	11 / 4	2 / 2	0.77
PAD / Buerger's disease (%)	10 / 5	4 / 0	0.48
Fontaine class	3.8 ± 0.4	4 ± 0	0.36
(Rutherford classification)	II-4 to IV-6	III-5 to IV-6	
Smoking (%)	13 (87)	2 (50)	0.36
Hypertension (%)	8 (53)	3 (75)	0.83
Diabetes mellitus (%)	7 (47)	3 (75)	0.66
Hemodialysis (%)	3 (20)	2 (50)	0.57
Aspirin (%)	6 (40)	3 (75)	0.5
Cilostazol (%)	7 (47)	1 (25)	0.83
ACE-I/ARB (%)	8 (53)	4 (100)	0.26
Calcium channel blocker (%)	5 (33)	3 (75)	0.35
β-blocker (%)	3 (20)	1 (25)	0.64
Statin (%)	6 (40)	2 (50)	0.83
Insulin (%)	3 (20)	0 (0)	0.84
Fasting glucose (mg/dl)	107 ± 26.4	135 ± 88.0	0.28
HbA1c (%)	5.6 ± 0.7	5.6 ± 1.1	0.96
HDL-cholesterol (mg/dl)	41 ± 11	33 ± 3.9	0.17
LDL-cholesterol (mg/dl)	97 ± 26	54 ± 12	<0.01
Triglyceride (mg/dl)	115 ± 78.6	157 ± 149	0.45
Serum creatinine (mg/dl)	2.2 ± 3.1	6.1 ± 4.7	0.06
eGFR (mL/min per 1.73 m ²)	62 ± 41	14 ± 14	<0.05
CRP (mg/dl)	2.0 ± 2.4	1.0 ± 0.5	0.43

Data are shown as mean ± SD or number (%).

$eGFR (mL/min/1.73 m^2) = 194 \times \text{Serum creatinine}^{-1.094} \times \text{Age}^{-0.287}$ (Female $\times 0.739$)

PAD, peripheral artery disease; ACE-I, angiotensin converting enzyme inhibitor; ARB, angiotensin 1 receptor blocker; eGFR, estimated glomerular filtration rate; CRP, C-reactive protein

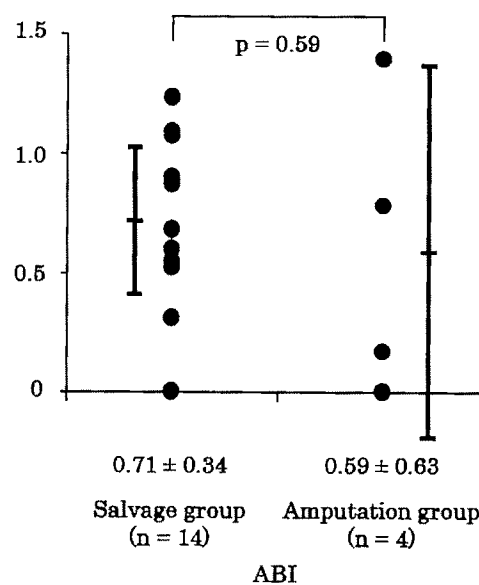


Fig. 1 Ankle brachial index before bone marrow cell implantation.

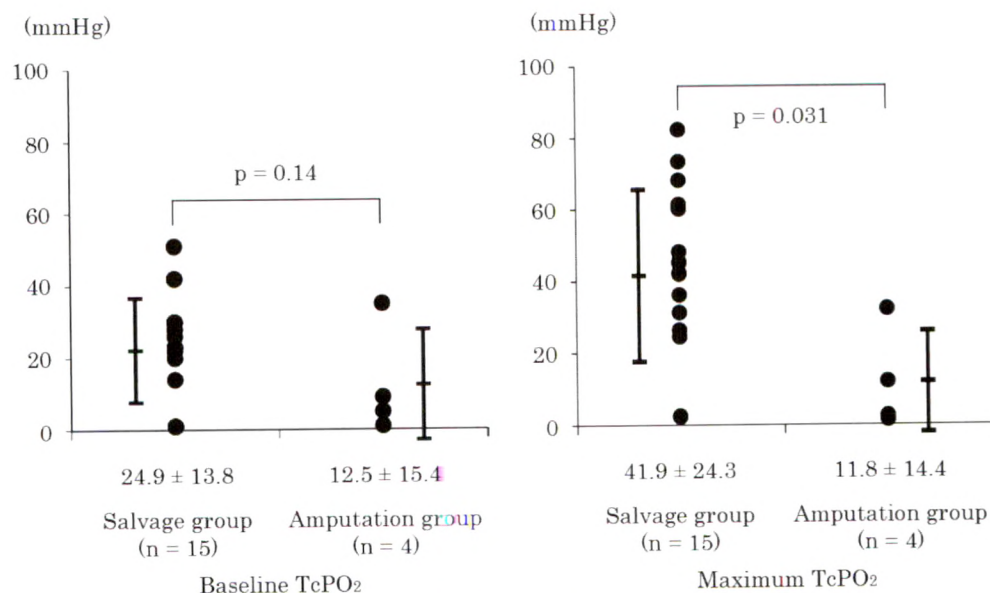


Fig. 2 Transcutaneous oxygen tension (TcPO₂) measurements at ambient conditions (A: baseline TcPO₂) and during 5 min of pure oxygen inhalation at 5 mL/min (B: maximum TcPO₂).



Fig 3 Representative image of ^{99m}Tc-TF perfusion scintigraphy. Arrow-heads indicate lower leg region, and arrows indicate foot region of ischemic leg.

CI 0.82–1.07; $p = 0.009$] for ^{99m}Tc-TF perfusion index in the foot region, suggesting high predictive accuracy of these parameters for limb salvage. The calculated best cut-off value was 18 mmHg for maximum TcPO₂ (sensitivity 0.87, specificity 0.75) and 0.65 for ^{99m}Tc-TF perfusion index in the foot region (sensitivity 0.77, specificity 1.0). **Fig. 5** illustrates major amputation-free survival

when the patients were divided into two groups by these cut-off values. Patients with maximum TcPO₂ and ^{99m}Tc-TF perfusion index in the foot region above the cut-off value had a significantly higher limb salvage rate than those whose measurements were below the cut-off value (log-rank test, $p = 0.008$, $p = 0.006$, respectively) (**Fig. 5**).

DISCUSSION

Because the major reason for amputation in CLI is an unhealed ulcer or gangrene, one of the important objectives of therapeutic angiogenesis is wound healing and prevention of ischemic ulcers. Therapeutic angiogenesis by BMCI is thought to improve the microcirculation, playing a crucial role in wound healing.¹²⁾ The possible mechanism is that bone marrow mononuclear cells consist of a variety of cell populations committed to vascular formation,¹³⁾ secretion of angiogenic cytokines,¹⁴⁾ and stimulation of muscle cells, promoting the secretion of angiogenic factors.¹⁵⁾

In the present study, the mean value of baseline TcPO₂ of all patients was 22 ± 15 mmHg, which was almost identical to the cut-off value for limb amputation previously reported.^{8, 12, 16)} Even for patients in this critical condition, we achieved a 79% limb salvage rate at 12 weeks of follow up after BMCI, indicating that BMCI could be used as a powerful strategy for CLI to salvage limbs

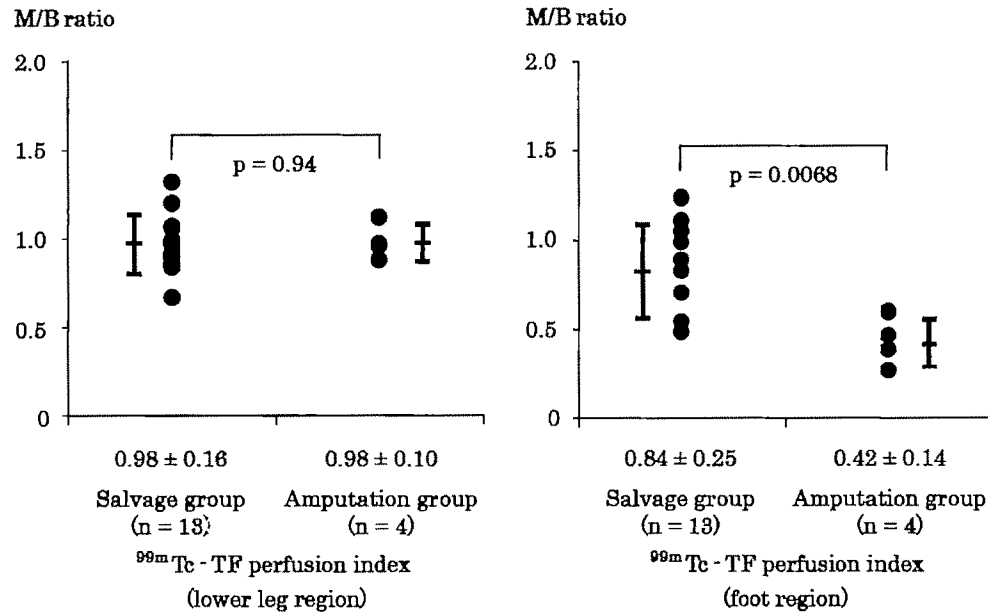


Fig. 4 Tissue blood flow estimated by ^{99m}Tc -TF perfusion scintigraphy (^{99m}Tc -TF perfusion index: expressed as muscle to brain [M/B] ratio of mean counts per pixel). Lower leg region (A) and foot region (B).

A | B

from major amputation.

In the present study, the value of TcPO_2 was significantly different between the two groups, only when taken during O_2 inhalation (maximum TcPO_2). Furthermore, the ROC curve analysis showed that maximum TcPO_2 is highly accurate in predicting limb salvage. It is reported that maximum TcPO_2 is a useful predictor of limb amputation in PAD,¹⁷⁾ and our data support this concept as well. The underlying mechanism is that maximum TcPO_2 could reveal the remaining potential of flow reserve which is masked under a normoxic condition, by increasing the arterial oxygen content.¹⁸⁾ Thus, maximum TcPO_2 rather than baseline TcPO_2 might represent the severity of ischemia more accurately.

In our previous investigation, the ^{99m}Tc -TF perfusion index was shown to be a useful examination to evaluate the increase in blood flow of the microcirculation in response to BMCI.⁵⁾ The usefulness of ^{99m}Tc -TF is supported by the following mechanism: 1) ^{99m}Tc emits high energy photons, enhancing image quality, and the shorter half-life allows administration of a higher dosage,¹⁹⁾ 2) ^{99m}Tc represents both blood flow perfusion and cellular viability, because uptake and retention are dependent on cell membrane integrity and mitochondrial function.^{19, 20)}

In the present study, we demonstrated that ^{99m}Tc -TF perfusion index in the foot region prior to BMCI was a

significant predictor to divide patients into a salvage group and an amputation group. Furthermore, ROC curve analysis indicated ^{99m}Tc -TF perfusion index in the foot region to have high predictive accuracy.

We showed the cut-off values of maximum TcPO_2 and ^{99m}Tc -TF perfusion index in the foot region for limb salvage, which was determined by ROC curve analysis, and subsequent Kaplan-Meier analysis revealed that these cut off values estimated chronological changes in limb salvage. These findings provide important clinical pre-cognition of responders to BMCI before treatment. Furthermore, to salvage the limbs of patients subjected to BMCI with values below the cut-off values, additional or alternative intervention may be required.

It was important to compare these cut-off values including the patients treated with conventional therapy. However, patients enrolled in this study were already scheduled to have a limb amputation, even before the consultation at our hospital. Thus, we could not randomize the patients to a BMCI treatment group versus a conventional treatment group, for ethical reasons. Even in such "no-option" patients, we encourage to find a possibility of limb salvage. Although clinicians who participate in the care of CLI sometime face an immediate decision of limb amputation, we believe that providing various treatment options for CLI would provide a better prognosis in CLI patients.

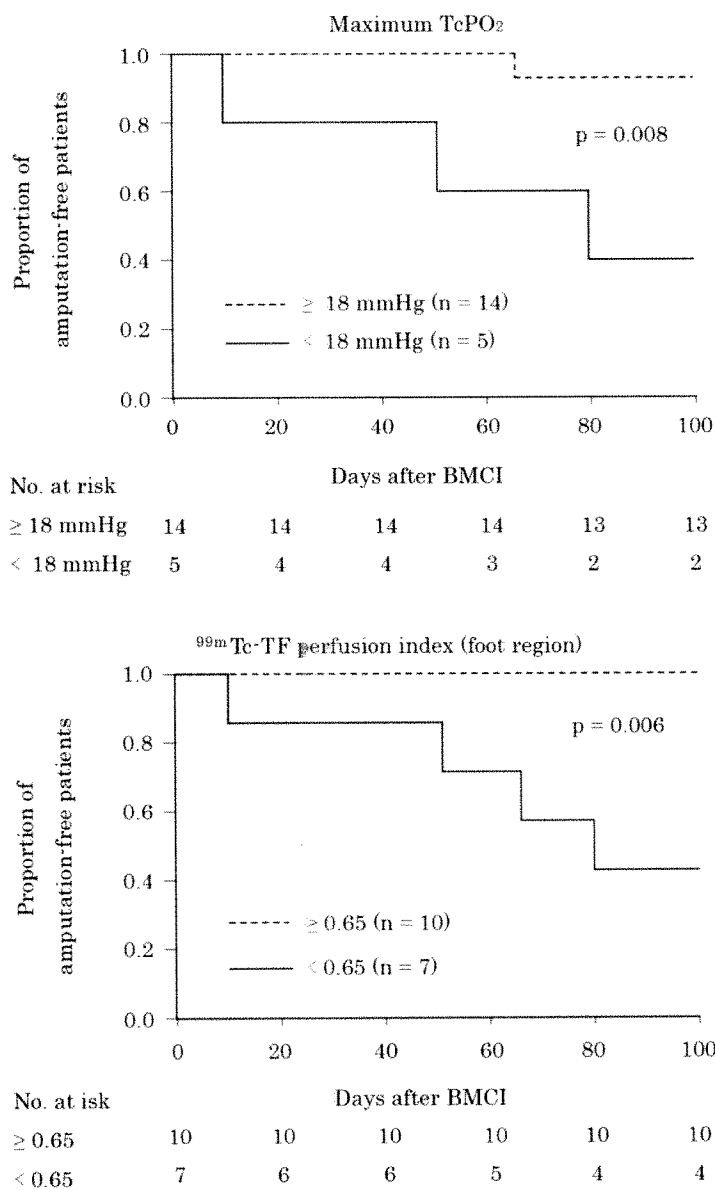


Fig. 5 Kaplan-Meier plots of time to major limb amputation dichotomized at the cut-off values of maximum TcPO₂ (A) and ^{99m}Tc-TF perfusion index in the foot region (B).

A
B

In the present study, there was no significant difference in ABI between the two groups. Although ABI is considered to be a useful method in the diagnosis of PAD, it does not represent blood flow of the microcirculation, which is an important factor in wound healing in CLI.¹²⁾ Besides, severe calcification causes a pseudo-normalized value, which may affect the accuracy of the evaluation of ischemic severity.

In summary, BMCI was performed in 19 CLI patients, and the limb salvage rate was 79%. Maximum TcPO₂ and ^{99m}Tc-TF perfusion index in the foot region are pre-

dictors of limb salvage after BMCI in CLI patients.

Study limitations

There are several limitations of the present study. First, this was a retrospective study with a small number of subjects. Therefore, multivariate analysis was not performed. For ROC curve analysis, the small number of outcomes made the curve rough. In addition, the cut-off values determined by this ROC curve analysis might be inadequate. Second, limb salvage was determined at 12 weeks of follow up after BMCI, which may be too short

a follow-up period. Third, blood concentration of LDL-cholesterol and estimated GFR at baseline were significantly higher in the salvage group than in the amputation group, suggesting that patient characteristics might also have influenced the outcome. The results of this study need to be confirmed in a large population.

REFERENCES

- 1) Hirsch AT, Haskal ZJ, Hertzner NR, Bakal CW, Creager MA, Halperin JL, et al. ACC/AHA 2005 guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): executive summary a collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease) endorsed by the American Association of Cardiovascular and Pulmonary Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; and Vascular Disease Foundation. *J Am Coll Cardiol* 2006; **47**: 1239–312.
- 2) Welten GM, Schouten O, Hoeks SE, Chonchol M, Vidakovic R, van Domburg RT, et al. Long-term prognosis of patients with peripheral arterial disease: a comparison in patients with coronary artery disease. *J Am Coll Cardiol* 2008; **51**: 1588–96.
- 3) Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG, et al. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). *Eur J Vasc Endovasc Surg* 2007; **33** (Suppl 1): S1–75.
- 4) Bertele V, Roncaglioni MC, Pangrazzi J, Terzian E, Tognoni EG. Clinical outcome and its predictors in 1560 patients with critical leg ischaemia. Chronic Critical Leg Ischaemia Group. *Eur J Vasc Endovasc Surg* 1999; **18**: 401–10.
- 5) Miyamoto M, Yasutake M, Takano H, Takagi H, Takagi G, Mizuno H, et al. Therapeutic angiogenesis by autologous bone marrow cell implantation for refractory chronic peripheral arterial disease using assessment of neovascularization by ^{99m}Tc-tetrofosmin (TF) perfusion scintigraphy. *Cell Transplant* 2004; **13**: 429–37.
- 6) Tateishi-Yuyama E, Matsubara H, Murohara T, Ikeda U, Shintani S, Masaki H, et al. Therapeutic angiogenesis for patients with limb ischaemia by autologous transplantation of bone-marrow cells: a pilot study and a randomised controlled trial. *Lancet* 2002; **360**: 427–35.
- 7) White RA, Nolan L, Harley D, Long J, Klein S, Tremper K, et al. Noninvasive evaluation of peripheral vascular disease using transcutaneous oxygen tension. *Am J Surg* 1982; **144**: 68–75.
- 8) Wyss CR, Matsen FA 3rd, Simmons CW, Burgess EM. Transcutaneous oxygen tension measurements on limbs of diabetic and nondiabetic patients with peripheral vascular disease. *Surgery* 1984; **95**: 339–46.
- 9) Amann B, Luedemann C, Ratei R, Schmidt-Lucke JA. Autologous bone marrow cell transplantation increases leg perfusion and reduces amputations in patients with advanced critical limb ischemia due to peripheral artery disease. *Cell Transplant* 2009; **18**: 371–80.
- 10) Kijima T, Kumita S, Cho K, Kumazaki T. ^{99m}Tc-tetrofosmin exercise leg perfusion scintigraphy in arteriosclerosis obliterans (ASO)—assessment of leg ischemia using two phase data acquisition. *Kaku Igaku* 1998; **35**: 305–13. (in Japanese)
- 11) Hanley JA, McNeil BJ. A method of comparing the areas under receiver operating characteristic curves derived from the same cases. *Radiology* 1983; **148**: 839–43.
- 12) Kalani M, Brismar K, Fagrell B, Ostergren J, Jorreskog G. Transcutaneous oxygen tension and toe blood pressure as predictors for outcome of diabetic foot ulcers. *Diabetes Care* 1999; **22**: 147–51.
- 13) Asahara T, Masuda H, Takahashi T, Kalka C, Pastore C, Silver M, et al. Bone marrow origin of endothelial progenitor cells responsible for postnatal vasculogenesis in physiological and pathological neovascularization. *Circ Res* 1999; **85**: 221–8.
- 14) Kamihata H, Matsubara H, Nishiue T, Fujiyama S, Tsutsumi Y, Ozono R, et al. Implantation of bone marrow mononuclear cells into ischemic myocardium enhances collateral perfusion and regional function via side supply of angioblasts, angiogenic ligands, and cytokines. *Circulation* 2001; **104**: 1046–52.
- 15) Tateno K, Minamino T, Toko H, Akazawa H, Shimizu N, Takeda S, et al. Critical roles of muscle-secreted angiogenic factors in therapeutic neovascularization. *Circ Res* 2006; **98**: 1194–202.
- 16) Takolander R, Rauwerda JA. The use of non-invasive vascular assessment in diabetic patients with foot lesions. *Diabet Med* 1996; **13** (Suppl 1): S39–42.
- 17) Harward TR, Volny J, Golbranson F, Bernstein EF, Fronek A. Oxygen inhalation—induced transcutaneous PO₂ changes as a predictor of amputation level. *J Vasc Surg* 1985; **2**: 220–7.
- 18) Scheffler A, Rieger H. Clinical information content of transcutaneous oxymetry (tcpO₂) in peripheral arterial occlusive disease (a review of the methodological and clinical literature with a special reference to critical limb ischaemia). *Vasa* 1992; **21**: 111–26.
- 19) Slart RH, Bax JJ, van Veldhuisen DJ, van der Wall EE, Dierckx RA, Jager PL. Imaging techniques in nuclear cardiology for the assessment of myocardial viability. *Int J Cardiovasc Imaging* 2006; **22**: 63–80.
- 20) Travin MI, Bergmann SR. Assessment of myocardial viability. *Semin Nucl Med* 2005; **35**: 2–16.

► **Original Article** ◀

Ten Years Experience of Aortic Root Replacement Using a Modified Bentall Procedure with a Carrel Patch and Inclusion Technique

Wataru Hashimoto, MD, Koji Hashizume, MD, Tsuneo Ariyoshi, MD, Shinichiro Taniguchi, MD,
Takashi Miura, MD, Tomohiro Odate, MD, Seiji Matsukuma, MD, Kazuki Hisatomi, MD, and Kiyoyuki Eishi, MD

Objective: A modified Bentall procedure with a Carrel patch and inclusion technique (Modified Bentall Procedure) has been used to treat combined disease of the aortic valve and aortic root. The current study examined the outcomes of this surgical technique.

Materials and Methods: Between April 1999 and March 2009, 16 patients (10 males, 6 females; 63.3 ± 9.4 years) underwent elective surgery involving the Modified Bentall Procedure and no additional surgery, so they were included in the study.

Results: The mean cardiopulmonary bypass time was 140.2 ± 34.4 min (range: 97–232 min), and aortic cross-clamp time was 97.3 ± 16.6 min (range: 76–132 min). There were no hospital deaths. No patients required additional surgery to correct excessive bleeding. The follow-up rate was 100% (16/16). The mean follow-up period was 5.6 ± 2.8 years (range: 0.7–9.9 years). One of the 16 patients died (6.3%) due to lung cancer, and 1 of the 15 surviving patients required additional surgery (6.7%) for a thoracic aortic aneurysm. Kaplan-Meier analysis found that 1-year and 5-year survival and event-free survival rates were all 100%.

Conclusions: The Modified Bentall Procedure provided satisfactory results over both the short term and long term.

Key words: aortic root replacement, modified Bentall procedure

INTRODUCTION

The surgical reconstruction of the aortic root with a valved composite graft was first reported by Bentall and De Bono.¹⁾ The reported disadvantages of the classical Bentall technique are excessive postoperative bleeding and pseudoaneurysm formation at the suture lines.^{2, 3)} Since its original development, the Bentall technique has

undergone several modifications.²⁾ The current group of investigators use the Modified Bentall Procedure, as reported by Kawazoe et al. in 1993.⁴⁾ The current study examined this surgical procedure and its outcomes.

MATERIALS AND METHODS

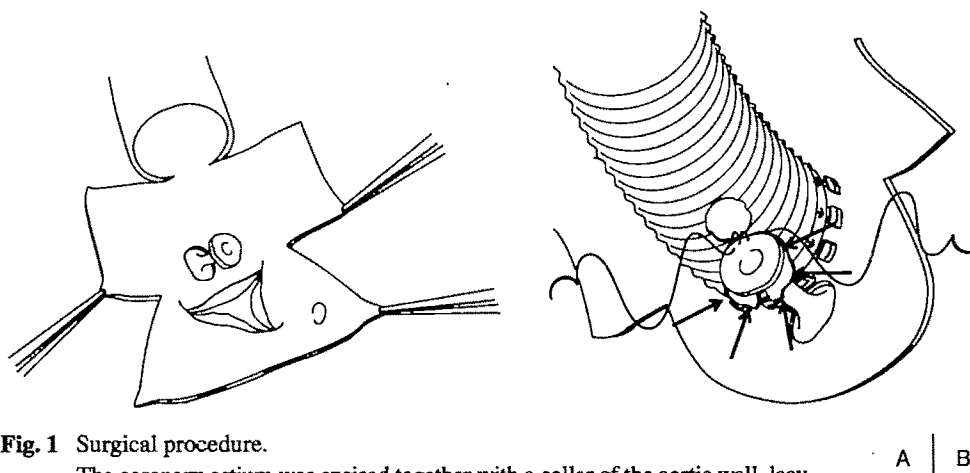
Between April 1999 and March 2009, 31 patients underwent aortic root replacement at Nagasaki University Hospital, Nagasaki, Japan. Sixteen of these patients (10 males, 6 females; mean age $\pm$ standard deviation (SD): 63.3 ± 9.4 years; range: 48–79 years) underwent elective surgery involving the Modified Bentall Procedure but no additional surgery, so they were included in the study. The patients' medical records were reviewed retrospectively to obtain data on patient demographics, symptoms, echocardiographic and computed tomographic findings,

Graduate School of Biomedical Science Division of Cardiovascular Surgery, Nagasaki University, Nagasaki, Nagasaki, Japan

Received: November 15, 2010; Accepted: December 1, 2010
Corresponding author: Wataru Hashimoto MD, Graduate School of Biomedical Science Division of Cardiovascular Surgery, Nagasaki University, 1-7-1 Sakamoto, Nagasaki, Nagasaki 852-8501, Japan
Tel: +81-95-819-7307, Fax: +81-95-819-7311
E-mail: coolcat_watawata0127@yahoo.co.jp

Table 1 Patient characteristics

	n = 16
Age	63.3 ± 9.4
Male/Female	10/6
Diagnosis	
AAE	12
Atherosclerotic aneurysm	2
Aneurysm of Valsalva	2
(Marfan syndrome)	3
(Previous surgery)	1
Ascending aorta diameter (mm)	59.1 ± 9.0
New York Heart Association Functional Class II / III	7/9

**Fig. 1** Surgical procedure.

The coronary ostium was excised together with a collar of the aortic wall, leaving epicardium on the aortic wall (A). The coronary button was attached in an end-to-side fashion to the composite graft using polypropylene running sutures reinforced by an autologous pericardium patch (arrows) (B).

surgical procedures, complications, and survival rates. Follow-up was performed via hospital visits and/or telephone interviews.

Preoperative characteristics

The preoperative characteristics of the patients are summarized in **Table 1**. Indications for surgery were annuloaortic ectasia in 12 patients, atherosclerotic aneurysm in 2 (1 of whom had undergone previous surgery), and aneurysm of the sinus of Valsalva in 2. Three of the 16 study patients had Marfan syndrome (18.8%). The average diameter of the ascending aorta was 59.1 ± 9.0 mm. All 16 patients had moderate or severe aortic regurgitation. Based on the New York Heart Association (NYHA) functional classification system, 7 patients (43.8%) were graded as Functional Class II at the time of

surgery, and 9 patients (56.3%) were Class III (mean class: 2.6 ± 0.3) (**Table 1**).

Surgical technique

Cardiopulmonary bypass was established using ascending aortic cannulation and right atrium drainage. After ventricular fibrillation was induced using a cardiac fibrillator, a venting cannula was placed into the right upper pulmonary vein. After cross-clamping of the ascending aorta, the aorta was transected, and then cold cardioplegic solution was injected into the coronary ostium. Using a hand-held cautery device, the coronary ostium was excised together with a 'collar'-like remnant of the aortic wall (extending 5 mm from the ostium), leaving epicardium on the aortic wall and further mobilizing the excised ostium and wall (**Fig. 1A**). Particular

attention was paid to avoiding perforation of the epicardium. After removal of the aortic valve, the optimal sizes of the prosthetic valve and graft were determined. The prosthetic valve was inserted into the graft (not fixed), and the valve and graft were implanted into the aortic annulus using everting mattress sutures (3-0 polyester suture). At this point in the surgical procedure, composite graft replacement was complete; therefore, a composite graft need not be created beforehand because it can be made intraoperatively using this technique. The current investigators use a biological replacement valve in patients of age 70 years and over. The left and then the right coronary buttons were attached in an end-to-side fashion to the composite graft using 5-0 polypropylene running sutures reinforced by an autologous pericardium patch (**Fig. 1B**). The distal end of the tubular graft was closed manually, and a cardioplegia cannula was inserted into the distal end of the graft. The aortic root and the coronary button anastomoses were checked for possible bleeding by high-pressure administration of a cardioplegic solution. Distal anastomosis of the graft to the transected aorta was performed using a continuous 4-0 polypropylene suture. During anastomosis, the suturing needle was inserted into the distal aortic wall from the outside and into the graft and the proximal aortic wall from the inside (three layers).

After the cross-clamp was removed, the aortotomy was closed during rewarming of the patient, and the graft was completely included after weaning of the patient from cardiopulmonary bypass.

Intraoperative characteristics

Ten patients received a Dacron composite graft with a mechanical valve, 5 received a Dacron composite graft with a biological valve, and 1 received a Carbo-Seal composite valve graft (Sulzer Carbomedics Inc, Austin, TX, USA). The mean operating time was 294.0 ± 59.0 minutes (range: 202–402 minutes), cardiopulmonary bypass time was 140.2 ± 34.4 minutes (range: 97–232 minutes), and aortic cross-clamp time was 97.3 ± 16.6 minutes (range: 76–132 minutes) (**Table 2**).

Follow-up

The follow-up rate was 100% (16/16 patients attended at least 1 annual hospital visit). The mean follow-up period was 5.6 ± 2.8 years (range: 0.7–9.9 years).

Statistical analysis

Survival and event-free survival curves were calcu-

Table 2 Operative data

Variables	Date
CPB duration (min)	140.2 ± 34.4 (97–232)
Aortic cross-clamp time (min)	97.3 ± 16.6 (76–132)
Post operative drainage (ml)	434.8 ± 247.5 (110–878)
Composite graft	No. of patients
ATS 21mm + 24mm	4
ATS 23mm + 26mm	4
ATS 25mm + 28mm	2
CEP 21mm + 24mm	3
CEP 23mm + 28mm	1
Mosaic 21mm + 24mm	1
Carbo-Seal 25mm	1

CPB, cardiopulmonary bypass; ATS, ATS bileaflet prosthesis; CEP, Carpentier-Edwards permount

Table 3 Results

Complications	No. of occurrences	%
Atrial fibrillation or flutter	6/16	37.5
Ventricular fibrillation	1/16	6.2
Respiratory failure	1/16	6.2
Additional surgery	1/15	6.7

lated using the Kaplan-Meier method. Data are presented as means $\pm$ SD, ranges, and percentages.

RESULTS

Short-term outcomes

There were no hospital deaths of patients in the study. None of the patients required additional surgery to correct excessive bleeding. The average volume of postoperative drainage was 434.8 ± 247.5 ml (range: 110–878 ml). The percentage of patients not requiring transfusion was 31.3% (5/16 patients). Postoperatively, atrial fibrillation or flutter occurred in 6 patients (37.5%). Ventricular fibrillation occurred in 1 patient (6.3%), and normal heart rhythm was restored electrically. One patient had postoperative respiratory failure requiring prolonged ventilation and a tracheostomy (**Table 3**).

Long-term outcomes

Of 16 patients, 1 patient died (6.3%) 5.5 years after surgery due to lung cancer. Therefore, based on Kaplan-Meier analysis, the 1-year and 5-year survival and event-free survival rates were all 100%. One of the 15 surviving patients required additional surgery (6.7%) for a thoracic aortic aneurysm (not a pseudoaneurysm) 7 years after the original surgery (Table 3). None of the study patients had an anticoagulant-related hemorrhage, valve thrombosis, coronary event, pseudoaneurysm, or prosthesis-related complication. All 16 patients underwent NYHA functional reclassification after surgery: 14 patients (87.5%) were graded as functional Class I, and only 2 patients (12.5%) were Class II (mean: 1.1 ± 0.3).

DISCUSSION

The Bentall procedure and its major modifications have been the technique of choice for composite graft replacement of the ascending aorta and aortic valve in the treatment of a variety of pathological conditions. The reported disadvantages of the classical Bentall technique are excessive postoperative bleeding and pseudoaneurysm formation at the suture lines.^{2,3} Therefore, it is crucial to control bleeding during a Bentall operation in order to reduce the time needed for hemostasis. Since 1999, the current investigators have used a modified Bentall procedure with a Carrel patch and inclusion technique, as reported by Kawazoe et al.⁴

Hospital mortality and morbidity

The advantages of performing the Bentall procedures with a Carrel patch are that coronary ostial reimplantation into the prosthetic graft can be easily performed with good visualization and that stress on the anastomosis can be avoided. Milano et al. noted that the formation of pseudoaneurysms at all sites of anastomosis of tissue to the conduit (including the aortic annulus, coronary ostia, and distal aorta) has been a troublesome late complication of the inclusion technique.⁵ Thus, to avoid anastomotic stress and bleeding, the coronary ostium can be detached to facilitate its mobility and then reinforced with autologous pericardium during anastomosis.⁴ Sokullu et al. also used Teflon felt to control bleeding during coronary artery anastomosis.⁶

When creating coronary buttons, it is essential to avoid injuring the epicardium so that eventually the graft can be wrapped completely (and any tears can be sutured in the event of epicardial damage). Complete coverage by

the epicardium serves to concentrate oozing from the needle hole in the wrapping and should reduce the time required for hemostasis and help control bleeding with a cell saver until protamine takes effect.

In the current study, the mean durations of aortic cross-clamping and cardiopulmonary bypass were 97.3 ± 16.6 and 140.2 ± 34.4 minutes, respectively. The average volume of postoperative blood drainage was 434.8 ± 247.5 ml (range: 110–878 ml). No patients required additional surgery to correct excessive bleeding. The percentage of patients not requiring transfusion was 31.3% (5/16 patients). There were no hospital deaths of study patients. Lewis et al. and Svensson et al. cited increased cardiopulmonary bypass time (≥ 163 minutes; odds ratio: 4.95) and aortic clamp time (≥ 98 minutes; odds ratio: 5.43) as factors associated with early mortality.^{3,7} The current study's modified Bentall technique proved effective in reducing the time needed for hemostasis, cardiopulmonary bypass duration, and aortic cross-clamp time.

Long-term survival and events

The Kaplan-Meier analysis confirmed that 1-year and 5-year survival and event-free survival rates were all 100%. One patient died of lung cancer 5.5 years after surgery. Another patient required additional surgery for a thoracic aortic aneurysm (not a pseudoaneurysm) 7 years after the original surgery. Kouchoukos et al.² and Yakut⁸ indicated that the incidence of a coronary ostial pseudoaneurysm when using a button technique varies from 3.1% to 9%, but the current study found no incidence of coronary pseudoaneurysm. Miller and Mitchell described the use of a doughnut of Teflon felt or autologous pericardium placed around the coronary ostial aspect of the coronary buttons to prevent tearing of tissues.⁹ Reinforcement with autologous pericardium during coronary artery anastomosis also prevented late pseudoaneurysm; however, pseudoaneurysms of coronary ostia anastomoses, as well as at the distal aortic suture line, have been observed.⁹

We use a biological valve for patients of age 70 years and older, and do not consider ongoing anticoagulation with warfarin to be necessary in these patients. None of the study patients suffered an anticoagulant-related hemorrhage or valve thrombosis. Numerous reports have indicated that a thromboembolic complication or anticoagulation-related hemorrhage is less likely with a biological valve.^{10–13} We consider composite graft root replacement to be the treatment of choice for many pathological conditions affecting the aortic root and aortic valve.

Yacoub et al.¹⁴⁾ and David et al.¹⁵⁾ reported on remodeling and reimplantation as new procedures for aortic root aneurysms; however, these procedures are limited to use in patients with normal valve leaflets. There are still concerns about the management of severe aortic regurgitation. The Modified Bentall Procedure, as we have described here, provided satisfactory results in terms of both surgical and long-term outcomes. Today, various techniques are available for aortic root reconstruction; however, as explained by Silva et al.¹⁶⁾ complicated surgery is not necessary for cases in which the Bentall procedure is likely to produce satisfactory results.

CONCLUSIONS

The current study found that the Modified Bentall Procedure provided satisfactory results in patients requiring aortic root replacement. Pseudoaneurysms, coronary events, and prosthesis-related complications were not observed.

REFERENCES

- 1) Bentall H, De Bono A. A technique for complete replacement of the ascending aorta. *Thorax* 1968; **23**: 338–9.
- 2) Kouchoukos NT, Wareing TH, Murphy SF, Perillo JB. Sixteen-year experience with aortic root replacement. Results of 172 operations. *Ann Surg* 1991; **214**: 308–20.
- 3) Lewis CT, Cooley DA, Murphy MC, Talledo O, Vega D. Surgical repair of aortic root aneurysm in 280 patients. *Ann Thorac Surg* 1992; **53**: 38–45.
- 4) Kawazoe K, Eishi K, Kawashima Y. New modified bentall procedure: Carrel patch and inclusion technique. *Ann Thorac Surg* 1993; **55**: 1578–9.
- 5) Milano D, Pratali S, Mecozzi G, Boraschi P, Brancini G, Magagnini E, et al. Fate of coronary ostial anastomoses after the modified Bentall procedure. *Ann Thorac Surg* 2003; **75**: 1797–802.
- 6) Sokullu O, Sanioglu S, Orhan G, Kut MS, Hastaoglu O, Karaca P, et al. New use of Teflon to reduce bleeding in modified Bentall operation. *Tex Heart Inst J* 2008; **35**: 147–51.
- 7) Svensson LG, Grawford S, Hess KR, Coselli JS, Safi HJ. Composite valve graft replacement of the proximal aorta: comparison of techniques in 348 patients. *Ann Thorac Surg* 1992; **54**: 427–39.
- 8) Yakut C. A new modified Bentall procedure: the flanged technique. *Ann Thorac Surg* 2001; **71**: 2050–2.
- 9) Miller DC, Mitchell RS. Composite aortic valve replacement and graft replacement of the ascending aorta plus coronary ostial reimplantation: how I do it. *Semin Thorac Cardiovasc Surg* 1993; **5**: 74–83.
- 10) Sioris T, David TE, Ivanov J, Armstrong S, Feindel CM. Clinical outcomes after separate and composite replacement of the aortic valve and ascending aorta. *J Thorac Cardiovasc Surg* 2004; **128**: 260–5.
- 11) Byrne JG, Gudbjartsson T, Karavas AN, Mihaljevic T, Phillips BJ, Aranki SF, et al. Biological vs. mechanical aortic root replacement. *Eur J Cardiothorac Surg* 2003; **23**: 305–10.
- 12) Hagl C, Strauch JT, Spielvogel D, Galla JD, Lansman SL, Squitieri R, et al. Is the Bentall procedure for ascending aorta or aortic valve replacement the best approach for long-term event-free survival? *Ann Thorac Surg* 2003; **76**: 698–703.
- 13) Settepani F, Eusebio A, Ornaghi D, Baebone A, Citterio E, Manasse E, et al. Aortic root replacement with the Carboseal composite valve graft: analysis of risk factors. *Interact CardioVasc Thorac Surg* 2005; **4**: 360–4.
- 14) Yacoub MH, Gehle P, Chandrasekaran V, Birks EJ, Child A, Radley-Smith R. Late results of a valve-preserving operation in patients with aneurysms of the ascending aorta and root. *J Thorac Cardiovasc Surg* 1998; **115**: 1080–90.
- 15) David TE, Feindel CM, Webb GD, Colman JM, Armstrong S, Maganti M. Aortic valve preservation in patients with aortic root aneurysm: results of the reimplantation technique. *Ann Thorac Surg* 2007; **83**: S732–5.
- 16) Silva VF, Real DSS, Branco JNRB, Catani R, Kim HC, Buffolo E, et al. Bentall and De Bono surgery for correction of valve and ascending aortic disease: long-term results. *Rev Bras Cir Cardiovasc* 2008; **23**: 256–61.

Case Report

Severe Limb Ischemia Related to Previous Abdominal Aortic Aneurysm Repair Induced by Acute Aortic Dissection

Yukio Umeda, MD, PhD, Matsuhisa Imaizumi, MD, PhD, Yoshio Mori, MD, PhD, and Hiroshi Takiya, MD, PhD

We described the first case of limb ischemia induced by acute aortic dissection in the patient with previous abdominal aortic aneurysm (AAA) repair. A 56-year-old male was referred for severe limb ischemia. He underwent AAA repair one month before the referral. Computed tomography (CT) scan revealed Stanford type B aortic dissection extended to the proximal anastomosis site of the AAA repair. The false lumen made the complete interruption of antegrade blood flow at the proximal anastomosis site of the AAA repair.

Key words: limb ischemia, abdominal aortic aneurysm repair, acute aortic dissection

INTRODUCTION

Several cases of limb ischemia induced by acute aortic dissection were previously reported, including a case with abdominal aortic aneurysm (AAA).¹⁻³⁾ On the other hand, limb ischemia related to aortic dissection at the site of aortic clamp or iliac artery is known as a complication of AAA repair.⁴⁾ However, severe limb ischemia induced by Stanford type B aortic dissection has not been described in a patient with previous AAA repair. In this paper, we described an unusual case of limb ischemia induced by acute aortic dissection in a patient with previous AAA repair.

CASE REPORT

A 56-year-old man was referred to our department for sudden onset of severe limb pain and paralysis of the limbs. He underwent AAA repair with a tube graft and reconstruction of the inferior mesenteric artery (IMA)

one month before the referral at our department; however, he had no history or symptoms of limb ischemia, and postoperative ankle brachial pressure (ABI) was normal (>1.0). Postoperative computed tomography (CT) scan also revealed no obvious problems at the anastomosis or aortic clamp site (Fig. 1a). The clinical course after AAA repair was uneventful, and he was discharged on postoperative day 9. Concerning the referral for severe limb pain, we investigated the pulse of the bilateral femoral arteries, which was not detectable. As for the ABI, Doppler sound was not also audible. The physical examination revealed paresthesia and paralysis of the lower extremity. Contrast media-enhanced CT scan revealed Stanford type B aortic dissection extended to the proximal anastomosis site of the AAA repair. Ulcer like projection (ULP) site suggesting that it was the primary tear was seen at the proximal descending aorta. False lumen of the aorta was totally occupied with thrombus except the ULP site. The false lumen made the complete interruption of antegrade blood flow at the proximal anastomosis site of the AAA repair (Fig. 1b, Fig. 2). The celiac trunk, the superior mesenteric artery, and the bilateral renal arteries were originated from true lumen; however, the origin of the left renal artery was narrowed by the false lumen. Distal lesion of the proximal anastomosis site was maintained by collateral circulation through the epigastric artery or the mesenteric artery system.

Emergency right axillo-bifemoral bypass was performed using an 8 × 7 mm bifurcated graft. Limb color,

Department of Cardiovascular Surgery, Gifu Prefectural General Medical Center, Gifu, Gifu, Japan

Received: December 2, 2010; Accepted: December 8, 2010
Corresponding author: Yukio Umeda, MD, PhD. Department of Cardiovascular Surgery, Gifu Prefectural General Medical Center, 4-6-1 Noishiki, Gifu, Gifu 500-8717, Japan
Tel: +81-58-246-1111, Fax: +81-58-248-3805
E-mail: yukioumeda@mvd.biglobe.ne.jp

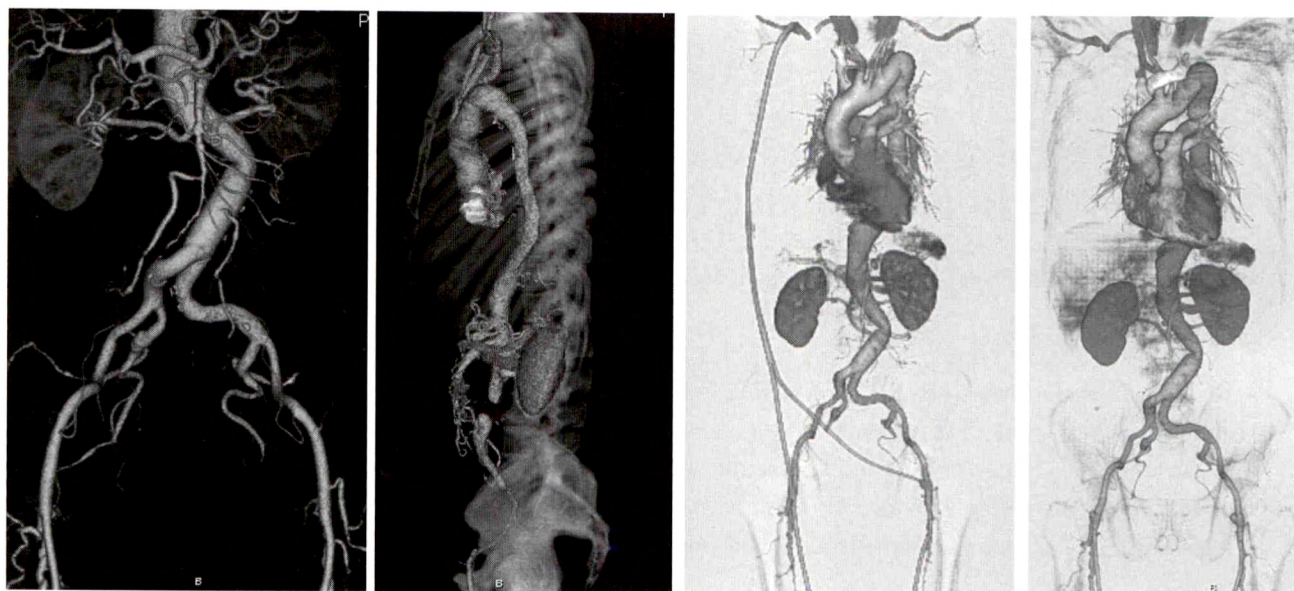


Fig. 1 Three-dimensional CT scan.
a: on the 7th day after AAA repair.
b: on referral for limb pain and paralysis.
c: on the 7th days after axillo-bifemoral bypass.
d: at 6 months after operation.
 CT, computed tomography

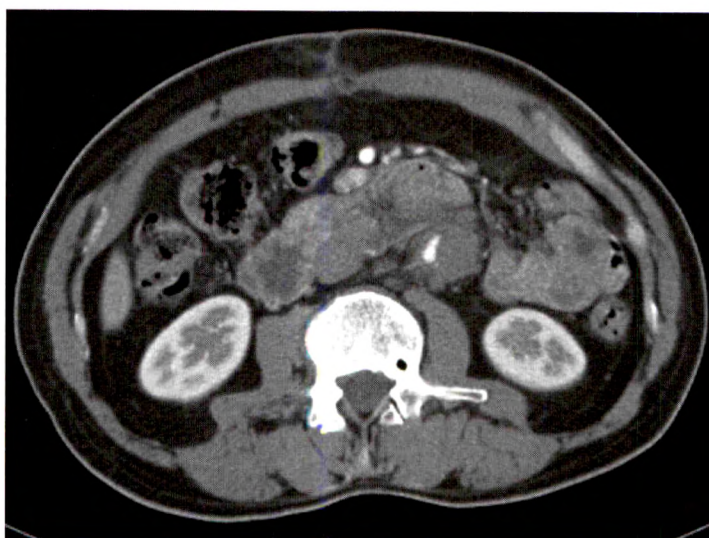


Fig. 2 Two-dimensional CT scan on referral for limb pain and paralysis.
 CT, computed tomography

ABI, and neurological dysfunction were improved immediately after operation. Postoperative significant elevation of serum creatine phosphokinase (CPK, peak CPK 16959 IU/l on IPOD) and transient elevation of creatinine (Cr, peak Cr 1.37 mg/dl on IPOD) were observed but improved steadily. Contrast media-enhanced CT scan on postoperative day 7 revealed the patent vascular prosthesis and the

persistent but reduced thrombosed false lumen of the aorta (**Fig. 1c**). The patient began to walk on postoperative day 7 according to the rehabilitation program for acute aortic dissection. His postoperative course was uneventful and he discharged on postoperative day 36. Contrast media-enhanced CT scan at 6 months after operation revealed occlusion of the axillo-bifemoral bypass graft and disap-

pearance of the false lumen (**Fig. 1d**). Sufficient antegrade blood flow to the lower extremity and normal ABI (>1.0) were also confirmed.

DISCUSSION

Limb ischemia is one of well-known complication of acute aortic dissection.¹⁻³⁾ We described the severe limb ischemia induced by aortic dissection in the patient with previous AAA repair. In our case, the totally thrombosed false lumen made the complete interruption of antegrade blood flow at the proximal anastomosis site. As far as we searched, there was no report of severe limb ischemia induced by aortic dissection in the patient with previous AAA repair. We should consider this because termination of the aortic dissection at the proximal anastomosis site of AAA repair is thought to be a major cause of limb ischemia. Furthermore, limb ischemia in the patient with previous AAA repair could be more severe than that in the patient without previous AAA repair because of reduced collateral circulation related to intra-operative closure of the lumbar arteries or un-reconstruction of the IMA or the internal iliac artery. In our institution, we reconstruct the IMA independent with the result of pressure measurement except the patients with the occluded IMA. In the present case, several pairs of the lumbar arteries were closed, but the internal iliac arteries were patent because of the tube graft repair and the IMA was reconstructed. Nevertheless, our case presented paralysis of the limbs at the same time with the onset of limb pain. This suggests the severity of ischemia induced by aortic dissection in the patient with previous AAA repair and the necessity of prompt and appropriate treatment.

With regards to severe ischemic cases, surgical procedure such as axillo-bifemoral bypass or femoro-femoral bypass has been carried out. Recently, endovascular repair of aortic dissection presenting as severe limb ischemia was also reported.^{5,6)} As a result of those appropriate treatments for limb ischemia, major limb amputation could be avoided in many cases. In our case, the proximal anastomosis site of AAA repair was close to major branches of the abdominal aorta. There was a risk of thromboembolism from the thrombosed false lumen. Thus, we judged that endovascular repair was inappropriate and decided to perform the extra-anatomical bypass grafting.

Limb color, ABI, and paralysis were improved immediately after operation. Postoperative significant elevation of CPK and transient renal dysfunction were observed but improved steadily. Postoperative clinical course was uneventful. At 6 months after operation, disappearance of aortic dissection and restart of antegrade blood flow were observed. Occlusion of the vascular prosthesis was also observed without any clinical symptom, such as intermittent claudication or thromboembolism.

We routinely reconstruct the IMA, independent of its pressure measurements because ischemia or necrosis of the large intestine may occur in a few patients who have had a reconstruction of their bilateral internal iliac arteries. In addition, we usually recommend the IMA reconstruction because it can help in the collateral circulation for improving lower-limb ischemia, induced by acute aortic dissection after AAA repair.

Here, we described an unusual case of limb ischemia induced by acute aortic dissection in the patient with previous AAA repair.

REFERENCES

- 1) Afán J, Shipolini A, Kyriakides C. A rare case of type A aortic dissection presenting as acute lower limb ischaemia. *Eur J Vasc Endovasc Surg* 2004; **27**: 563-4.
- 2) Farber A, Lauterbach SR, Wagner WH, Cossman DV, Long B, Cohen JL, et al. Spontaneous infrarenal abdominal aortic dissection presenting as claudication: case report and review of the literature. *Ann Vasc Surg* 2004; **18**: 4-10.
- 3) Iino M, Kuribayashi S, Takamiya M, Hamada S, Imakita S. A case of DeBakey type IIb acute aortic dissection extending through an atherosclerotic abdominal aortic aneurysm. *Nippon Igaku Hoshasen Gakkai Zasshi* 1996; **56**: 985-7. (in Japanese)
- 4) Haimovici H. Haimovici's vascular surgery: principles and techniques, 3rd ed. Cambridge, MA: Blackwell Science 1989; pp 370-85.
- 5) Adam DJ, Roy-Choudhury S, Bradbury AW. Endovascular repair of spontaneous infrarenal aortic dissection presenting as severe lower extremity ischaemia. *Eur J Vasc Endovasc Surg* 2007; **34**: 699-701.
- 6) Kurimoto Y, Morishita K, Kawaharada N, Osawa H, Maeda T, Higami T, et al. Immediate endovascular stent-grafting for leg ischemia secondary to acute aortic dissection: report of a case. *Ann Vasc Surg* 2007; **21**: 515-8.

» **Case Report** «

Balloon-trapped Technique for Successful OptEase Filter Retrieval

Katsuhiro Kondo, MD, Hirotoishi Watanabe, MD, Masashi Iwabuchi, MD, and Masakiyo Nobuyoshi, MD

Purpose: To describe a case of successful retrieval of OptEase filter, using the balloon-trapped technique, after failure of its retrieval by the standard techniques.

Case report: An 82-year-old man had an inferior vena cava filter placed for deep venous thrombosis prophylactically. Seven days after successful catheter-directed thrombolysis, the filter was retrieved after changing the position to caudal, using a standard angioplasty balloon. The patient was discharged on warfarin anticoagulant.

Conclusion: Balloon-trapped removal of the OptEase filter that failed standard retrieval attempt is an effective and safe technique that can be performed using commonly available tools and familiar to most interventionalists.

Key words: deep venous thrombosis, pulmonary embolism, permanent/retrieval filter, catheter-directed thrombolysis

INTRODUCTION

The relationship between deep venous thrombosis (DVT) and subsequent development of pulmonary embolism (PE) is well established and placement of a permanent inferior vena cava (IVC) filter is more effective in preventing symptomatic PE than anticoagulation alone.¹⁾ However, patients who had permanent IVC filters have an increased risk of lower limb DVT with no survival benefit.²⁾ So optional IVC filters are recommended, since they can be removed or left in the vena cava permanently.³⁾

Retrieval of vena cava filters is a valuable addition to the management of DVT. However, retrieval failure occurs due to technical difficulties. This is a case of successful retrieval of OptEase filter using the balloon-

trapped technique after failure of the standard retrieval techniques.

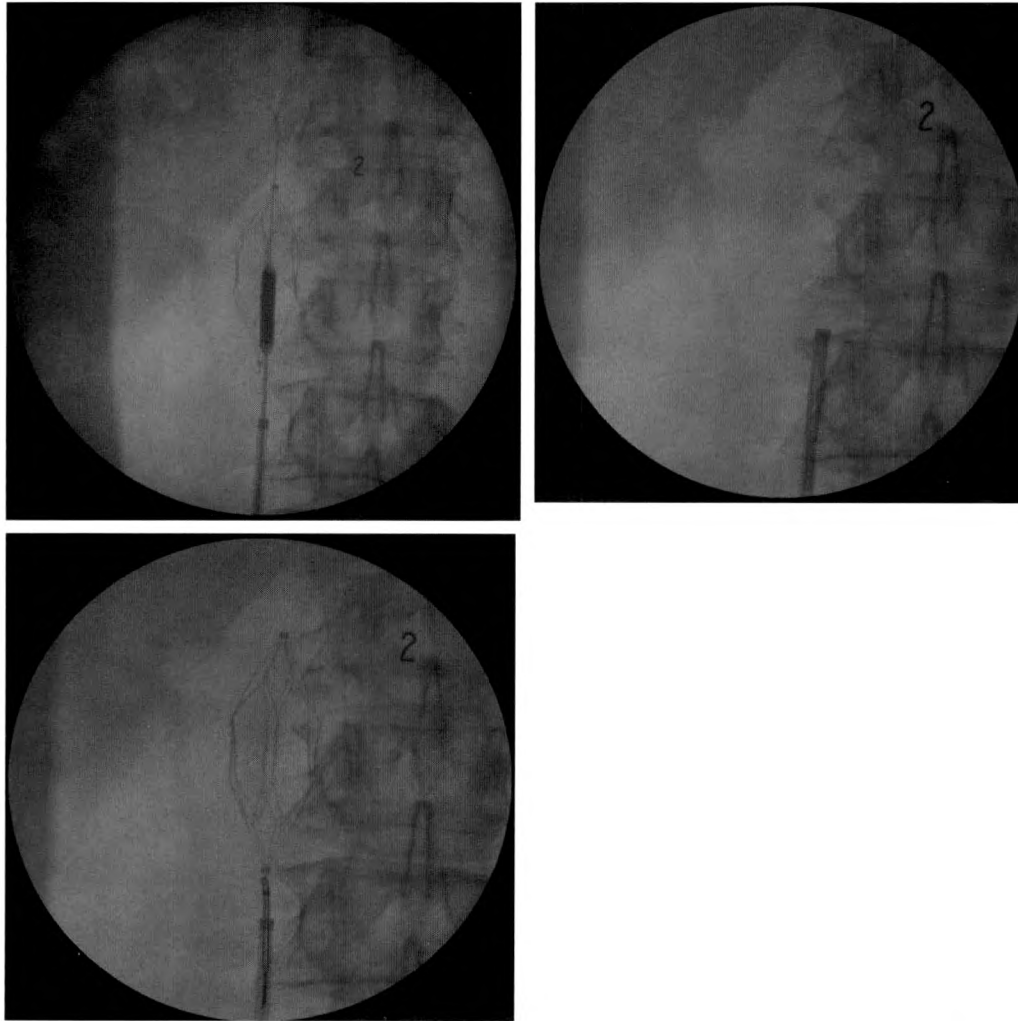
CASE

An 82-year-old man presented with acute onset of swelling and pain of his left leg. Computed tomography revealed proximal DVT. He was administered a therapeutic dose of heparin, but the symptoms continued to worsen. Catheter-directed thrombolysis was performed, and then an OptEase filter was placed prophylactically against PE.

Seven days after successful catheter-directed thrombolysis, we tried to retrieve the IVC filter. After sterile preparation and draping of the patient, local anesthetic (1% Lidocaine) was injected in the right groin. Then, the right femoral vein was cannulated using 10 French sheath (23 cm, Cordis) using Seldinger technique. The standard technique of retrieval was tried several times, but it failed to catch the hook of the filter. Therefore, we used the buddy wire technique⁴⁾ for IVC filter retrieval; however, we were not successful in its retrieval. So, the failure was thought to occur because the hook of the filter was close to the vena caval wall. An angled guide wire (0.035 inch, Terumo) was passed through the filter and then a 4.0 mm

Department of Cardiology, Kokura Memorial Hospital, Kitakyushu, Fukuoka, Japan

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Corresponding author: Katsuhiro Kondo, MD. Department of Cardiology, Kokura Memorial Hospital, 3-2-1 Asano, Kokurakita-ku, Kitakyushu, Fukuoka 802-8555, Japan
Tel: +81-93-511-2000, Fax: +81-93-511-2029
E-mail: seichan12257260@yahoo.co.jp

**Fig. 1****A:** Trapped balloon.**B:** Catching the filter's hook.**C:** The filter was removed by using the standard technique after changing its position.

A	C
B	

(diameter) by 20mm (length) over-the-wire type percutaneous transluminal angioplasty (PTA) balloon (Synergy™, Boston Scientific, USA) was delivered between the struts of the basket filter. After that, the balloon was inflated at nominal pressure to trap it between the struts of the lower basket. After that, the filter was moved about 10mm by pulling the trapped balloon catheter, the guiding catheter, and guide wire in the downward direction (**Fig. 1A**). After changing the position of the filter, we deflated the PTA balloon catheter and removed it with a guidewire. Then the filter was removed successfully using the standard technique (**Fig. 1B** and **1C**). The procedure did not result in any complications. The patient was discharged under Warfarin sodium treatment.

DISCUSSION

IVC filter placement in patients with DVT with or without pulmonary embolism protects against short-term and long-term development of PE. However, permanent filter placement can result in chronic complications such as filter occlusion and increased risk of DVT. The Prevention du risque d'embolie pulmonaire par interruption cave (PREPIC) study suggests that in the case of patients in whom short-term prevention of PE is required, it might be more attractive to use a retrievable filter over a permanent one, since it helps avoid the long-term complications associated with a permanent filter.^{1, 2)} Therefore, the demand for retrievable IVC filters, which have high

rates of successful retrieval, has increased.³⁾

Currently, the following 3 retrievable IVC filters for temporary insertion are available in Japan: Günther Tulip filter (Vena Cava MReye Filter Set, William Cook Europe); ALN filter (ALN Implants Chirurgicaux, Ghisonaccia, France); and OptEase filter (Cordis, Roden, Netherlands). Retrieval failure due to technical reasons is a commonly occurring problem. In case of the use of optional filters other than the OptEase filter, particularly in the case of the Günther Tulip filter, numerous reports have been published on alternative techniques (e.g., snare-over-guidewire loop technique).⁴⁻⁶⁾

Failure to retrieve the OptEase filter owing to technical reasons has been reported in 2 cases by using the expression "potentially retrieval" filter.⁷⁾ The structural design of the OptEase filter facilitates retrieval since the retrieval hook is supposed to be at the center of the IVC. However, in some cases, as in the case of lumbar scoliosis, the course of IVC may be curved. Therefore, in such cases, the retrieval hook may be in contact with the IVC wall, thereby making filter retrieval impossible. One possible means of resolving this problem is using the buddy wire technique. In this technique, a stiff guidewire is passed through the OptEase filter and positioned parallel to the major axis of the vena cava. In this way, the retrieval hook is separated from the venous wall, thus enabling easier snaring; this appears to be a simple and effective technique. However, in practice, the operator should have some level of experience or skill to perform this technique successfully.

In balloon trapping presented in this report, a guidewire is passed through the OptEase filter, and then the PTA balloon is inflated between the upper and lower baskets. Then, the trapped balloon in the lower basket is pulled downward to change the position of the filter, thus enabling snaring of the retrieval hook. In this technique, the guidewire can be easily passed, and complex manipulation is not required, as opposed to that in the buddy wire technique in which the wire needs to be passed through the opposite side of the upper region after passage between the hook and the adjacent venous wall. One advantage of pulling in the downward direction is prevention of injury to the IVC wall caused by the upward directed barbs of the OptEase filter, which are designed to provide resistance to migration. Moreover, this maneuver enables the guiding catheter to be as close as possible

to the filter, thereby resulting in safer filter retrieval.

This technique enabled safe and reliable retrieval of the filter after the filter could not be retrieved by applying the standard technique. Moreover, the retrieved filters were intact. This technique is promising because it is simpler, more reliable, and safer than the buddy wire technique for filter retrieval. Balloon trapping is an alternative technique that can be used by interventionalists who are unfamiliar with the buddy wire technique. To the best of our knowledge, we may be the first to use balloon trapping in the successful retrieval of the OptEase filter.

In case of failure of the standard technique for OptEase filter retrieval, balloon trapping is an effective and a safe retrieval technique that can be performed using commonly available tools and is familiar to most interventionalists.

REFERENCES

- 1) Decousus H, Leizorovicz A, Parent F, Page Y, Tardy B, Girard P, et al. A clinical trial of vena cava filters in the prevention of pulmonary embolism in patients with proximal deep-vein thrombosis. Prevention du Risque d'Embolie Pulmonaire par Interruption Cave Study Group. *N Engl J Med* 1998; **338**: 409-15.
- 2) PREPIC Study Group. Eight-year follow-up of patients with permanent vena cava filters in the prevention of pulmonary embolism: the PREPIC (Prevention du Risque d'Embolie Pulmonaire par Interruption Cave) randomized study. *Circulation* 2005; **112**: 416-22.
- 3) Hoppe H. Optional vena cava filters. Indications, management and results. *Dtsch Arztebl Int* 2009; **106**: 395-402.
- 4) Pfammatter T, Hechelhammer L, Pfiffner R. "Buddy Wire" technique for successful OptEase filter retrieval. *J Vasc Interv Radiol* 2009; **20**: 656-9.
- 5) Kuo WT, Bostaph AS, Loh CT, Frisoli JK, Kee ST. Retrieval of trapped Günther Tulip inferior vena cava filters: snare-over-guide wire loop technique. *J Vasc Interv Radiol* 2006; **17**: 1845-9.
- 6) Burke CT, Dixon RG, Stavas JM. Use of rigid bronchoscopic forceps in the difficult retrieval of the Günther Tulip vena cava filter. *J Vasc Interv Radiol* 2007; **18**: 1319-23.
- 7) Kumar BC, Chakraverty S, Zeally I. Failed retrieval of potentially retrievable IVC filters: a report of two cases. *Cardiovasc Intervent Radiol* 2006; **29**: 126-7.

» **Case Report** «

Histopathologic Characteristics of a Coronary-pulmonary Artery Fistula with a Coronary Artery Aneurysm

Noriyuki Sakata, MD,¹ Noritoshi Minematsu, MD,² Noritsugu Morishige, MD,² Tadashi Tashiro, MD,² and Yoshinobu Imanaga, MD³

Here, we report a case of a 59-year-old woman with a coronary-pulmonary artery fistula with a concomitant coronary artery aneurysm, which comprised an anomalous coronary artery originating at the right coronary cusp, an aberrant branch of the left anterior descending artery, and a coronary artery aneurysm draining into the main pulmonary artery. Histopathologically, non-dilated anomalous coronary artery showed the preservation of internal elastic lamina and medial smooth muscle cell phenotype which lacked in the aneurysmal wall. Thus, the disrupted internal elastic lamina and phenotypic change of medial smooth muscle cells might contribute to aneurysm formation in a coronary-pulmonary arterial fistula.

Key words: coronary-pulmonary artery fistula, coronary artery aneurysm, histology, immunohistochemistry

INTRODUCTION

Coronary artery fistulas are uncommon congenital anomalies, first reported by Krause¹⁾ in 1865, and are characterized by the involved coronary artery having a normal origin from the aorta, but with a fistulous communication with either the cardiac chambers or another vascular structure, including the pulmonary artery and the superior vena cava. They are recognized more often with the improvement in diagnostic techniques, including selective coronary arteriography, echocardiography, and computed tomography. Although a coronary artery aneurysm associated with a fistula may result secondarily from atherosclerotic changes or traumatic injury to the fistula, it is even more rare than coronary artery fistulas.^{2, 3)} The clinicopathologic characteristics of a coronary

artery fistula concomitant with a coronary artery aneurysm are poorly understood because of their rarity.

In the present report, we describe the clinical, histological, and immunohistochemical characteristics of a coronary-pulmonary artery fistula concomitant with a coronary artery aneurysm. We also discuss the mechanisms potentially responsible for this lesion.

CLINICAL SUMMARY

A 59-year-old woman had a history of chest compression 6 years earlier. She has suffered from chest compression more frequently, and a heart murmur was detected at another hospital several months earlier. She was referred to our hospital because of chest compression and heart murmur. Her heart rate was 65 beats/min, and blood pressure was 131/86 mmHg. A continuous murmur of Levine III/VI was heard from the third intercostal space to the left sternal border. An electrocardiogram showed normal rhythm and no significant ST-T changes. An echocardiogram demonstrated an abnormal coronary artery. As shown in **Fig. 1**, multislice computed tomography revealed an anomalous coronary artery originating from the right coronary cusp (RCC) (indicated by No. 1 in **Fig. 1**) and an aneurysm formation (indicated by No.2 in **Fig. 1**). There was also an aberrant branch of the left anterior descending artery connecting to the aneurysm.

¹Department of Pathology, Faculty of Medicine, Fukuoka University, Fukuoka, Fukuoka, Japan

²Department of Cardiovascular Surgery, Faculty of Medicine, Fukuoka University, Fukuoka, Fukuoka, Japan

³Department of Nephrology, Asakurakensei Hospital, Asakura, Fukuoka, Japan

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Corresponding author: Noriyuki Sakata, MD. Department of Pathology, Faculty of Medicine, Fukuoka University, 45-1, 7-chome Nanakuma, Jonan-ku, Fukuoka, Fukuoka 814-0180, Japan
Tel: +81-92-801-1011, Fax: +81-92-865-9901

E-mail: nysakata@fukuoka-u.ac.jp

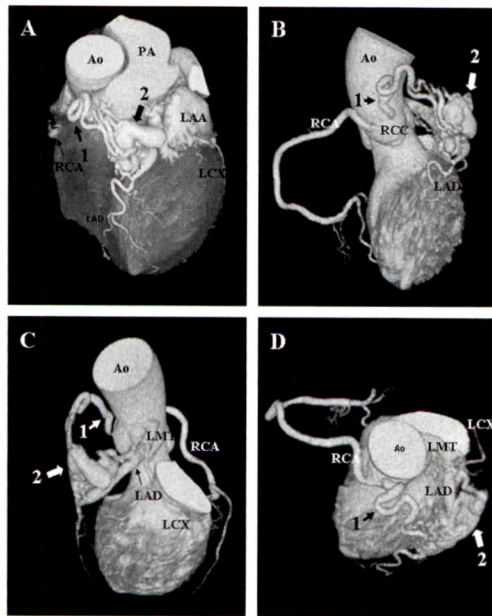


Fig. 1 The reconstructed images of multislice computed tomography show the coronary-pulmonary artery fistula, which comprises an anomalous coronary artery originating from the right coronary cusp (indicated by No. 1) and a concomitant aneurysm (indicated by No. 2) to the pulmonary artery and an aberrant branch of the left anterior descending artery.
Ao, aorta; PA, pulmonary artery; RCA, right coronary artery; RCC, right coronary cusp; LAD, left anterior descending artery; LCX, left circumflex coronary artery

Selected coronary angiography showed that the aneurysm received blood flow from the anomalous coronary artery and aberrant branch of the left anterior descending artery. Selected coronary angiography showed that the aneurysm received blood flow from the anomalous coronary artery and aberrant branch of the left anterior descending artery, which drained into the main pulmonary artery. On these findings, we diagnosed a coronary-pulmonary artery fistula with concomitant coronary aneurysm.

The patient underwent resection of the coronary-pulmonary artery fistula with the concomitant coronary aneurysm. The postoperative course was uncomplicated, and the patient remains asymptomatic.

MATERIALS AND METHODS

The pathologic specimen was fixed in 10% formalin and routinely processed for light microscopic and immunohistochemical examination. Paraffin-embedded serial sections were prepared and stained with hematoxylin-eosin, elastica van Gieson, Masson-Trichrome, Alcian

Table 1 Antibodies and staining methods used for immunohistochemistry

Antibody	Clone	Source	Dilution	Antigen retrieval method
CD34	QBEnd-10	Dako	1:100	Microwave heating
α SMA	1A4	Dako	1:100	Microwave heating
Desmin	D33	Dako	1:50	Microwave heating
Calponin	CALP1	Dako	1:800	Microwave heating

α SMA, smooth muscle actin; Dako, Glostrup, Denmark

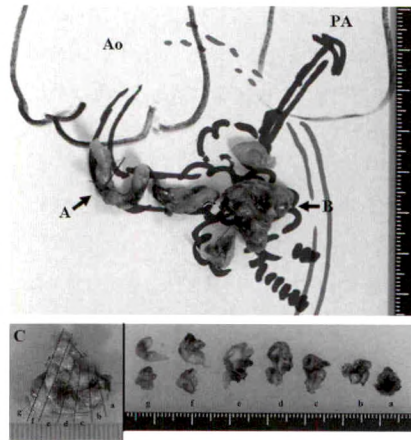


Fig. 2 Macroscopic view of the coronary-pulmonary artery fistula with a concomitant aneurysm. A: anomalous coronary artery; B: aneurysmal vessels; a–g in C: cut surface of aneurysmal vessels.
Ao, aorta; PA, pulmonary artery

blue-PAS, and Gram and PAS stains for light microscopic observation. Some sections were examined immunohistochemically with an indirect method, using the primary antibodies listed in Table 1.

All tissue specimens were taken in accordance with the protocol of the Human Research Subject Committee of the Fukuoka University School of Medicine.

PATHOLOGIC FINDINGS

The surgical specimen comprised a complex of a single anomalous coronary artery generating from the aorta (Fig. 2A) and abnormal vascular channels (Fig. 2B). The latter showed aneurysmal dilatation, up to 6 × 8 mm in diameter, depicted by d, e, and f in Fig. 2C. These aneurysmal vessels connected to the main pulmonary artery and aberrant branch of the left anterior descending artery. As shown in Fig. 3A, 3C, and 3D, the anomalous coronary artery showed mild intimal thickening and duplication of the internal elastic lamina, which was completely disrupted at the neck of the aneurysm. The tunica media

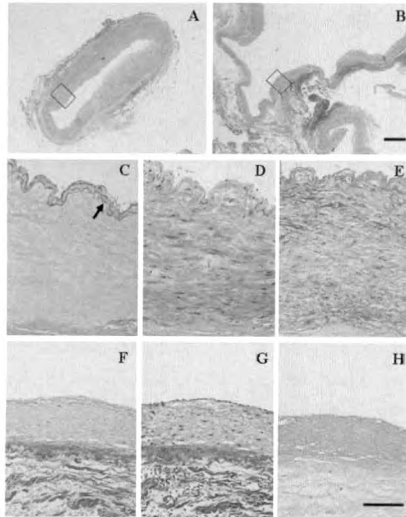


Fig. 3 Histologic features of the anomalous coronary artery (A, C–E) and concomitant aneurysm (B, F–H). A, B: Low-power view, hematoxylin-eosin staining, Bar = 50 μ m. C–E and F–H: High-power views corresponding to the boxed area in panel A and B, respectively. Arrow indicates the duplication of the internal elastic lamina in the anomalous coronary artery (Panel C). C, F: elastica van Gieson staining; D, G: Masson-Trichrome staining; E, H: Alcian blue-PAS staining. Bar = 100 μ m

of this artery was composed of densely packed, spindle-shaped smooth muscle cells. On the other hand, the aneurysmal vessels had a thin cellular wall with lack of the internal elastic lamina (**Fig. 3B, 3F, and 3G**). Alcian blue stained the entire wall of these vessels more strongly than the wall of the anomalous coronary artery (**Fig. 3E and 3H**). Atheromatous plaque was not found in either the anomalous coronary artery or aneurysmal vessels. There was no evidence of bacterial or fungal infection with Gram and PAS staining, respectively. Immunohistochemical staining showed the aneurysmal wall to be composed primarily of α SMA/calponin-positive and desmin-negative spindle cells (**Fig. 4F, 4G, and 4H**) that were similar to intimal cells of the coronary artery. In contrast, the medial smooth muscle cells of the anomalous coronary artery were positive for not only α SMA but also calponin and desmin (**Fig. 4B, 4C, and 4D**). A CD34-positive endothelium was found on the inner surface of the coronary artery and aneurysmal vessels (**Fig. 4A and 4E**).

DISCUSSION

Coronary artery fistulas are uncommon congenital abnormalities which are seen in 0.1% to 0.2% of patients

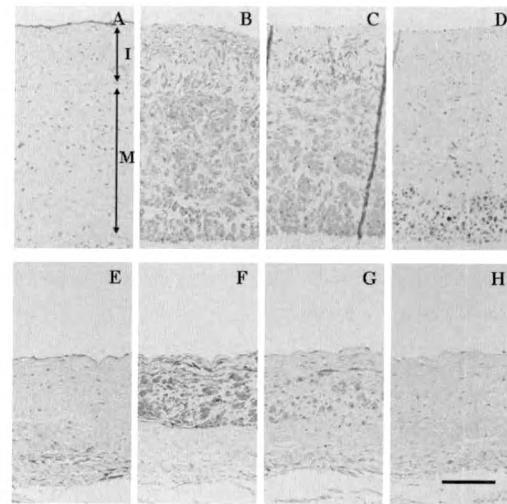


Fig. 4 Immunohistochemically determined patterns of CD34 (A, E), α SMA (B, F), calponin (C, G), and desmin (D, H) expressions. The anomalous coronary artery is shown in panels A–D, and the concomitant aneurysm in panels E–H. The medial smooth muscle cells of the anomalous coronary artery are positive for α SMA, calponin, and/or desmin, and the intimal smooth muscle cells are positive for α SMA and calponin but negative for desmin (B–D). The spindle cells in the aneurysmal wall are seen as positive for α SMA and calponin but negative for desmin (F–H). The CD34-positive endothelium is found on the inner surface of the anomalous coronary artery and concomitant aneurysm (A, E).

I, intima; M, media
Bar = 100 μ m

who underwent coronary angiography.⁴⁾ The coronary fistulas originated from the right coronary artery (55%) or left coronary artery (35%) but may arise from both coronary arteries (5%) and the anomalous single coronary artery (3%). They drain into the low-pressure chambers, including the right ventricle (42%), right atrium (34%), pulmonary artery (15%), and left atrium (5%).⁵⁾ The vessel wall of the coronary fistulas comprise a thick muscular media layer and well-defined internal elastic lamina, which are characteristic of the artery.⁵⁾ The present case demonstrated the complex of a single anomalous coronary artery with the histology of an artery originating from the RCC and aneurysmal vessels draining into the main pulmonary artery. A coronary artery aneurysm is considered a dilatation of a part of a coronary artery of more than 1.5 times the diameter of the adjoining coronary artery.⁷⁾ In the present case, the aneurysmal vessels were up to 6 $\times$ 8 mm in diameter, which was about twice as large as that of the anomalous coronary artery. The aneurysmal vessels had a thin cellular wall with a lack of

arterial histology. These findings suggest the present case to be a coronary artery fistula with a concomitant coronary artery aneurysm.

Complications associated with coronary artery fistulas include aneurysmal formation and rupture, congestive heart failure, myocardial ischemia, and endocarditis. An aneurysmal formation is quite rare and seems to exist in 26% of patients with a coronary arteriovenous fistula.⁸⁾ The causes of a coronary aneurysm concomitant with coronary artery fistulas are considered to be atherosclerotic, traumatic, and mycotic.⁹⁾ In our case, an atheromatous plaque was not found in either the anomalous coronary artery or the aneurysm. There was no evidence of bacterial or fungal infection in the aneurysmal wall. Atrophy and destruction of the musculo-elastic elements of the vessel wall can promote the formation of aneurysms.^{10), 11)} The anomalous coronary artery showed a well-defined internal elastic lamina and a thick muscular layer, which was immunohistochemically characterized by the positivity for α SMA, calponin, and desmin. In contrast, the aneurysm comprised a thin cellular wall with a lack of internal elastic lamina, abundant mucopolysaccharides and SMA/calponin-positive and desmin-negative spindle cells. These changes of the histochemical architectures may contribute to the formation of an aneurysm associated with a coronary-pulmonary artery fistula.

Smooth muscle internal scaffolding cytoskeleton comprises three classes of filamentous assemblies, including actin microfilaments, intermediate filaments and microtubules. In vascular smooth muscle cells, proteins in the intermediate filaments are mostly desmin and vimentin, which interact with the actin microfilaments.¹²⁾ Contractile elements in the smooth muscle actin network play a role in the mechanical properties of the cell. In the present study, we detected vimentin in the anomalous coronary artery and aneurysmal wall (data not shown). On the other hand, desmin was expressed in the former, but not in the latter. However, we found actin-associated proteins, including SMA and HHF35 (data not shown) in both. We suggest that intermediate filament-associated proteins, especially desmin, in smooth muscle cells are expressed differently in the anomalous coronary artery and aneurysmal wall.

In summary, we described the histopathologic characteristics of a coronary-pulmonary artery fistula with a concomitant aneurysm in a patient who had a history of chest compression and heart murmur. We discussed a potential mechanism for the development of a coronary artery aneurysm associated with the fistula.

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REFERENCES

- 1) Krause W. Über den Ursprung einer akzessorischen a. coronaria cordis aus der a. pulmonis. *Z Rationelle Med* 1865; **24**: 225.
- 2) Hirose H, Amano A, Yoshida S, Nagano T, Sunami H, Takahashi A, et al. Coronary artery aneurysm associated with fistula in adults: Collective review and a case report. *Ann Thorac Cardiovasc Surg* 1999; **5**: 258–64.
- 3) Hirooka K, Hanatani A, Nakatani S, Yoshimura Y, Bando K, Miyatake K, et al. Huge saccular aneurysm in a coronary-pulmonary fistula fed by the left and right coronary arteries. *Circ J* 2002; **66**: 525–7.
- 4) Darwazah AK, Hussein IH, Hawari MH. Congenital circumflex coronary arteriovenous fistula with aneurysmal termination in the pulmonary artery. *Tex Heart Inst J* 2005; **32**: 56–9.
- 5) Akashi H, Tayama E, Tayama K, Furunaga S, Tobinaga S, Sakashita H, et al. Rupture of an aneurysm resulting from a coronary artery fistula: a case report. *Circ J* 2003; **67**: 551–3.
- 6) Gobel FL, Anderson CF, Baltaxe HA, Amplatz K, Wang Y. Shunts between the coronary and pulmonary arteries with normal origin of the coronary arteries. *Am J Cardiol* 1970; **25**: 655–1.
- 7) Syed M, Lesch M. Coronary artery aneurysm: a review. *Prog Cardiovasc Dis* 1997; **40**: 77–84.
- 8) Said SA, el Gamal MI. Coronary angiographic morphology of congenital coronary arteriovenous fistulas in adults: a report of four new cases and review of angiograms of fifteen reported cases. *Cathet Cardiovasc Diagn* 1995; **35**: 29–35.
- 9) Imren Y, Zor H, Koksall P, Halit V. Giant aneurysm of left anterior descending coronary artery treated by surgical off-pump therapy. *Thorac Cardiovasc Surg* 2006; **54**: 349–52.
- 10) Chamberlain MH, Henry R, Brann S, Angelini GD. Surgical management of a gigantic circumflex coronary artery aneurysm with fistulous connection to the coronary sinus. *Eur J Cardiothorac Surg* 2001; **20**: 1255–7.
- 11) Takemura Y, Hirata Y, Sakata N, Nabeshima K, Take-shita M, Inoue T. Histopathologic characteristics of a saccular aneurysm arising in the non-branching segment of the distal middle cerebral artery. *Pathol Res Pract* 2009 Oct 2 [Epub ahead of print]
- 12) Johansson B, Eriksson A, Virtanen I, Thornell LE. Intermediate filament proteins in adult human arteries. *Anat Rec* 1997; **247**: 439–48.

Case Report

Ruptured Tuberculous False Aneurysm of the Abdominal Aorta: A Case Report

Alae Mechchat, Brahim Lekehal, Abbes Mesnaoui, Fannid Ammar, and Younes Bensaid

Tuberculous false aneurysm of the aorta is rare and has an unpredictable complication of aneurysm rupture. We report a case of a 32-year old woman who was referred to the Department of Vascular Surgery, Avicenne Hospital for severe abdominal pain. Chest x-ray revealed millary tuberculosis. Contrast enhanced computed tomography (CT) scan showed a false aortic aneurysm involving the juxtarenal aorta. Antituberculous treatment was started because of high presumption of tuberculosis. Five days later, the patient presented with symptoms of aneurysm rupture. She underwent an emergency a surgical resection of the aneurysm with repair of the aortic wall defect by a Dacron Silver patch. The histopathologic examination of the aortic wall showed features of tuberculosis.

Key words: aneurysm, aorta, tuberculosis

INTRODUCTION

Tuberculous aortic aneurysms are rare. Less than one hundred cases have been reported in the literature since 1952.¹⁾ The unpredictable complication is aneurysm rupture. We report a case of a ruptured tuberculous false aneurysm of the juxtarenal aorta associated with a pulmonary miliary. The patient underwent a successful excision and in-situ repair of the lesion and application of a prosthetic patch associated with antituberculous chemotherapy.

CASE REPORT

A 32-year-old woman was referred to the Department of Vascular Surgery, Avicenne Hospital for severe backache and abdominal pain for 2 weeks. She reported a history of fever, night sweats, anorexia, and weight loss of 8

kg over 4 months. She had no history of tuberculosis or contact with patients with tuberculosis. Physical examination revealed swelling in an epigastric mass, blood pressure of 120/80 mmhg, and temperature of 38.5°. Laboratory results showed a WBC of $20 \times 10^9/L$, hemoglobin 120 mg/L, and platelets of $230 \times 10^9/L$. Renal, hepatic, lipid, and coagulation profiles were normal. Chest x-ray revealed miliary tuberculosis (**Fig. 1**). The contrast enhanced CT scan showed a leaking aortic aneurysm involving the juxtarenal aorta measuring 7 cm/5 cm with thrombosis of the left renal artery and a mute left kidney (**Fig. 2**). Serology for human immunodeficiency virus and syphilis was non-reactive. We suspected tuberculosis and began antituberculosis chemotherapy. After 5 days, pain and pallor of the patient were greater, and the blood analysis revealed anaemia (8 g/dL of hemoglobin). The patient was taken to surgery, where she underwent a retroperitoneal approach extended through the 11th left intercostal space. We controlled the distal thoracic aorta first and then removed the retroperitoneal hematoma. The non functional kidney was removed. After excising the pseudo aneurysms, we closed the aortic wall defect with a Dacron Silver patch (**Fig. 3**). Postoperative recovery was uneventful, and the patient was discharged from the hospital on the seventh postoperative day. The histopathologic examination of the aortic wall showed evident features of tuberculosis.

Department of vascular surgery, Avicenne Hospital, Rabat, Morocco

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Corresponding author: Alae Mechchat. Department of Vascular Surgery, Avicenne Hospital, internat de l'hôpital Avicenne, 10000, Rabat, Morocco

Tel: 00212611863462, Fax: 00212537673551

E-mail: alae_mechchat@yahoo.fr

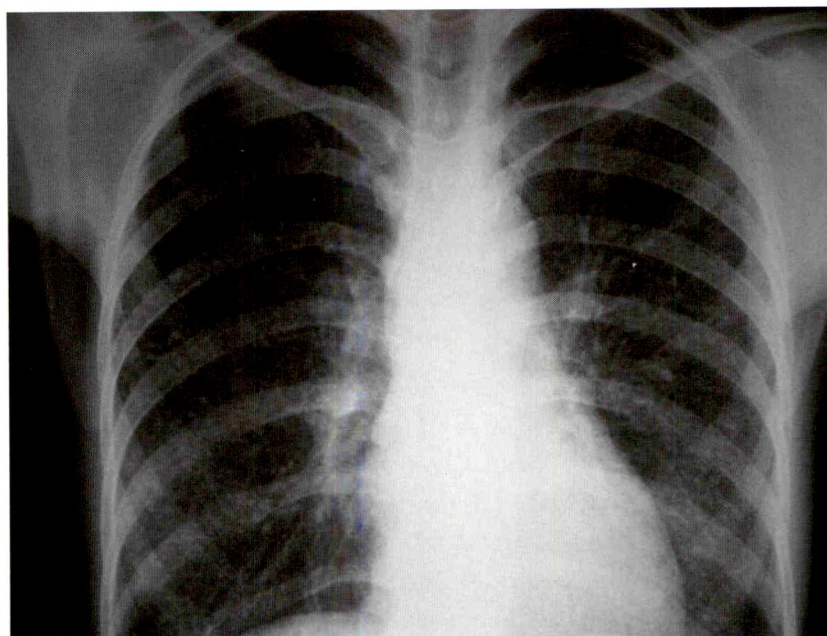


Fig. 1 Chest x-ray showing miliary tuberculosis.

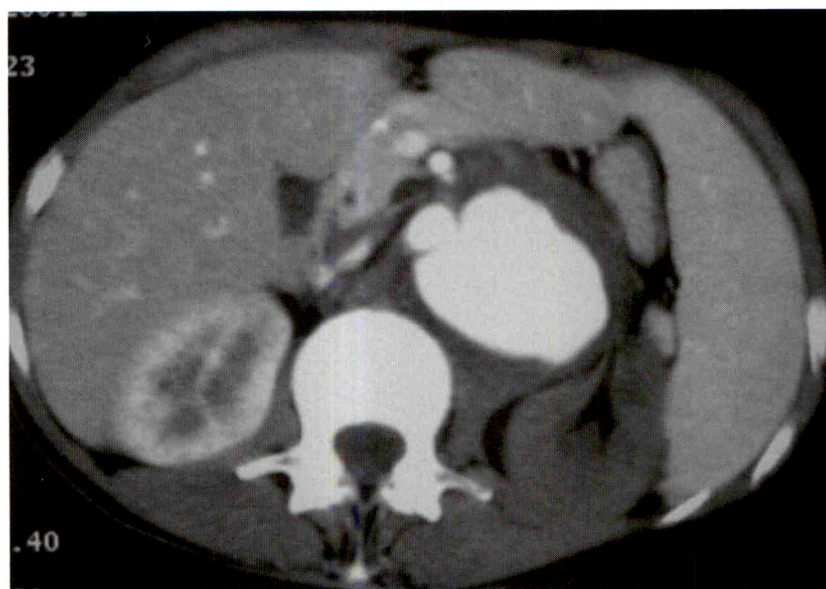


Fig. 2 Contrast enhanced CT scan showing a false aneurysm involving the juxtarenal aorta with thrombosis of the left renal artery and a mute left kidney.
CT, computed tomography

DISCUSSION

Tuberculous aortitis was first described by Weigert in 1882.²⁾ An infectious aortic aneurysm usually results from a transmural perforation of the aortic wall caused by direct extension from a contiguous infectious focus, usually lymphadenitis. Direct hematogenous invasion of

the vasa vasorum is rare and usually does not produce an aneurysm, as described in this case.³⁾ Most tuberculous aneurysms are false. However, when they are detected, they are most often saccular and rarely dissecting. A patient with tubercular aneurysms of the aorta may present with pain, a swollen mass of the para-aorta or symptoms of hemorrhagic shock, associated with typical



Fig. 3 Surgical view showing repair of the aortic wall defect with a silver dacron patch.

tuberculous symptoms or not, as in the patient presented here. Computed tomography (CT) with 3D reconstructions is the investigation of choice because it allows a better view of the size and the location of the aneurysm, thus enabling the physician to more easily determine the aetiology of infection and location of aneurysm rupture. In contrast, biological analysis points to mycobacterium tuberculosis. Because of the nature of this disease and the uniformly fatal outcome, early surgical resection in combination with perioperative antitubercular therapy offers the only chance for patient survival. Currently, endovascular repair with a stent graft was proposed by some authors, as long as the safety of the intervention was reviewed during 12-, 18- and 24- month follow-up visits.⁴⁻⁶⁾

CONCLUSION

Tuberculous aortic aneurysms usually present as rapidly growing or ruptured pseudoaneurysms. Surgery or endovascular repair should not be delayed.

REFERENCES

- 1) Herndon JH, Galt J, Austin DJ. Ruptured tuberculous false aneurysm of the abdominal aorta. *Tex State J Med* 1952; **48**: 336-8.
- 2) Weigert C. Über venetuberkel und ihre beziehung zur tuberkulosen blutinfektion. *Virchows Arch Pathol Anat* 1882; **88**: 307-9.
- 3) N.Sekar. Primary aortic infections and infected aneurysms. *Ann Vasc Dis* 2010; **3**: 24-7.
- 4) Steichen O, Pellerin O, Frank M, Emmerich J, Sapoval M, Fiessinger J-N, et al. Endovascular repair of a tuberculous aortic false aneurysm. *Rev Med Interne* 2007; **28**: 196-8.
- 5) Liu WC, Kwak BK, Kim KN, Kim SY, Woo JJ, Chung DJ, et al. Tuberculous aneurysm of the abdominal aorta: Endovascular repair using stent grafts in two cases. *Korean J Radiol* 2000; **1**: 215-8.
- 6) Semba CP, Sakai T, Slonim SM, Razavi MK, Kee ST, Jorgensen MJ, et al. Mycotic aneurysms of the thoracic aorta: repair with use of endovascular stent grafts. *J Vasc Intervent Radiol* 1998; **9**: 33-40.

» **Case Report** «

Usage of External Shunt in Hybrid Approach for Aortic Arch Aneurysm to Restore Cerebral Oxygenation

Hiroshi Mitsuoka, MD, PhD,¹ Hidekazu Furuya, MD,² Yoshinaga Nakao, MD, PhD,²
Tsunehiro Shintani, MD, PhD,¹ and Shigeki Higashi, MD, PhD²

A hybrid approach, combining open and endovascular procedures, may be a less invasive substitute to correct aortic arch pathologies in high-risk patients. We describe an 82-year-old male patient with an atherosclerotic aortic arch aneurysm, which was treated with proximal transposition of all arch branches and endovascular aortic arch repair. During the left common carotid artery reconstruction, oxygen saturation level of the left cerebral hemisphere decreased lower than the safety limit. To re-establish brain perfusion, we installed an external shunt from the right common femoral artery to the left common carotid artery. The oxygen saturation was restored to an acceptably safe level, and the patient tolerated the procedure without any signs of postoperative ischemic stroke.

Key words: aortic arch aneurysm, hybrid repair, ischemic stroke

INTRODUCTION

A hybrid approach, combining surgical and endovascular procedures, may be a less invasive substitute to correct aortic arch pathologies in high-risk patients.^{1, 2)} However, this technique does have some risks of fatalistic stroke, at least a small incidence of which may be cerebral ischemia during carotid artery clamping.³⁾ We describe a hybrid procedure for atherosclerotic aortic arch aneurysm. To maintain the tissue oxygen saturation level of the left hemisphere, we installed a bailout external shunt from the right common femoral artery (RCFA) during reconstruction of the left common carotid artery (LCCA). The patient tolerated the procedure without any signs of postoperative stroke.

¹Department of Vascular Surgery, Shizuoka Red Cross Hospital, Shizuoka, Shizuoka, Japan

²Department of Cardiac Surgery, Shizuoka Red Cross Hospital, Shizuoka, Shizuoka, Japan

Received: September 6, 2010; Accepted: January 5, 2011
Corresponding author: Hiroshi Mitsuoka, MD, PhD. Department of Vascular Surgery, Shizuoka Red Cross Hospital, 8-2 Otemachi, Aoi-ward, Shizuoka, Shizuoka 420-8630, Japan
Tel: +81-54-254-4311, Fax: +81-54-272-6983
E-mail: mitsuoka@SZRC.org

CASE REPORT

An 82-year-old male patient with a large atherosclerotic aortic arch aneurysm was referred to Shizuoka Red Cross Hospital. He had a long history of severe, chronic obstructive pulmonary disease. Because of the high surgical risks for conventional surgery (logistic Euroscore 29.21%),⁴⁾ a hybrid method, consisting of proximal transposition of all arch branches and endovascular aortic arch repair, was indicated. Throughout the procedure, the brain oxygenation was monitored by a transcranial near-infrared spectroscopy (INVOS, Somanetics Corporation, Troy, MI).

A woven Dacron bifurcated graft (10 × 8 × 8 mm, Gelsoft ERS, Terumo, Tokyo, Japan) was selected, and another 8 mm of Dacron graft (Gelsoft ERS, Terumo, Tokyo, Japan) was anastomosed to an 8 mm limb. We administered 5000 units of heparin, applied a partially occluding clamp to the lateral curve of the ascending aorta, and anastomosed the 10-mm limb of the prepared graft. The LCCA was clamped, transected at the arch, and sutured proximally. The lateral limb of the graft was anastomosed in an end-to-end configuration. Two minutes after we had clamped the LCCA, the oxygen saturation level of the left cerebral hemisphere decreased to lower than the safety limit (36%).^{5, 6)} To re-establish brain

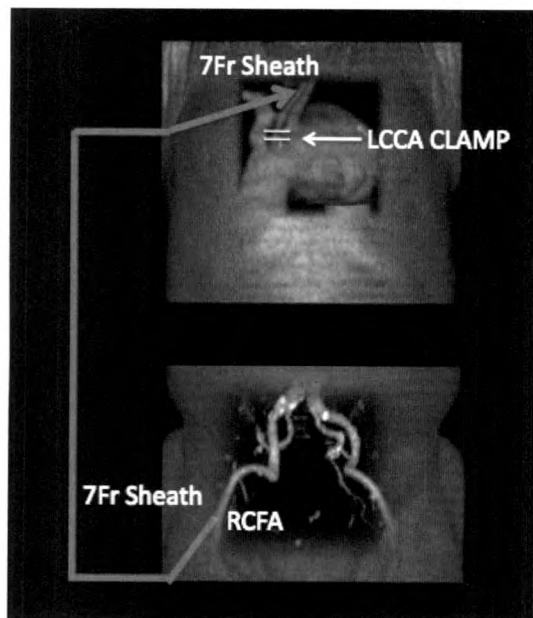


Fig. 1 An external shunt installed from the right femoral artery to left common carotid artery. An external shunt was established between the side ports of 7 Fr introducer sheaths, using a plastic tube. LCCA, left common carotid artery; RCFA, right common femoral artery

perfusion, we installed an external shunt from the RCFA to the LCCA. For a source of oxygenated blood, the side port of a 7 Fr introducer sheath, which had been inserted to the RCFA for the endovascular access, was selected. Another 7 Fr sheath was inserted to the LCCA (**Fig. 1**). The shunt restored the oxygen saturation to an acceptably safe level (**Fig. 2**). After the completion of anastomosis, the LCCA sheath was removed. The puncture site was corrected by closing a small size of purse string suture. The innominate artery (INA) was similarly addressed, using the other 8 mm lateral limb. Another 8 mm limb was anastomosed to the left axillar artery (LAA) in an end-to-side fashion. During INA and LAA reconstruction, the brain oxygen saturation levels remained in a safe range. The TAG endoprosthesis (W.L. Gore & Associates, Flagstaff, AZ) was introduced from the RCFA and positioned distally to the suture line of the bifurcated graft. The left subclavian artery was coil-embolized, using platinum-tungsten alloy coils (Interlock fibered IDC occlusion system, Boston Scientific Corporation, Natick, MA). A final angiogram found no signs of endoleak (**Fig. 3A**). The patient tolerated the entire procedure and showed no signs of ischemic stroke postoperatively. Three-dimensional computed tomography (CT)

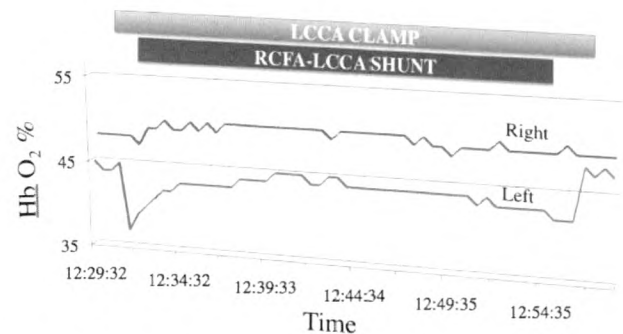


Fig. 2 Tissue hemoglobin oxygen saturation levels during left common carotid artery reconstruction. Tissue hemoglobin oxygen saturation levels (Hb O₂ %) in the left and right hemispheres were monitored by a transcranial near-infrared spectroscopy. LCCA, left common carotid artery; RCFA, right common femoral artery

at the third postoperative month found no signs of endoleak (**Fig. 3B**).

DISCUSSION

The mortality rate of conventional surgery for aortic arch aneurysm in high-risk patients is not negligible.⁷⁾ One possible alternative may be the above-mentioned hybrid procedure. Although it has an acceptably low rate of procedure-associated death, the main drawback of the method may be its causing cerebrovascular accidents.³⁾ The etiology of intraoperative stroke may be ischemic or embolic. Atherosclerotic debris can be released by surgical or endovascular procedures. Ischemic stroke results from inadequate cerebral perfusion related to flow cessation of carotid artery.

Empirically, a short period of arterial clamp during one side of carotid artery reconstruction does not decrease the brain oxygenation level severely. However, in the presence of extra- and intra-cranial arterial abnormality, even a few minutes of the flow cessation may cause a fatalistic degree of brain ischemia. A shunt tube for carotid endarterectomy (CEA) could have been used, if the remaining length of proximal carotid artery were long enough. Conversely, the length of remaining proximal LCCA was too short to use the shunt tube, especially in terms of sealing of arterial blood by inflating the proximal balloon. Therefore, the external arterial shunt, as described by Schönholz was employed as a bailout method.⁸⁾

The usage of temporal shunts has been a long-standing issue, especially related to CEA. Shunting is inherently

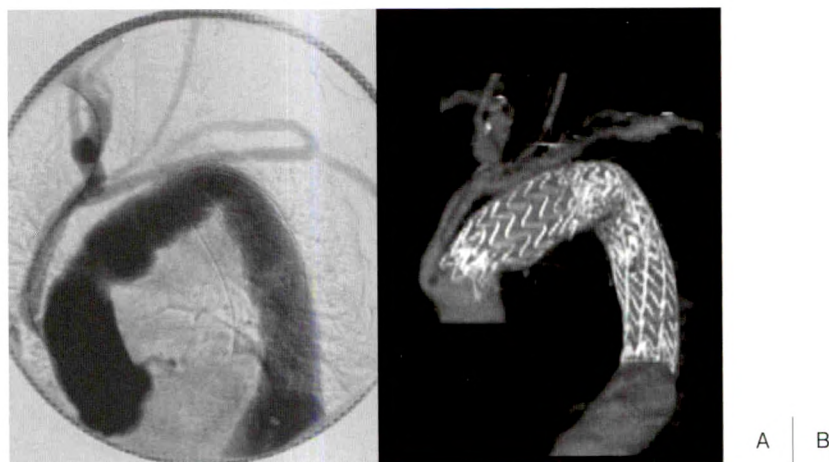


Fig. 3 Completion DSA (A) and three dimensional CT angiography (B). No signs of endoleak were detected in completion digital subtraction angiography (A) and three dimensional CT angiography at the third postoperative month.
CT, computed tomography

risky, because it may cause embolic stroke, as well as unpredicted adverse events related to the technical problem.⁹⁾ Controversies may exist in a decision-making about usage of external shunt under several methods of cerebral monitoring, including stump pressure (e.g. less than 50 mmHg), electroencephalogram (EEG) (e.g. at least 50% decrease in fast background activity), and INVOS (e.g. at least a 20% decrease from the background). Important thing is that none of these has complete accuracy in detecting intra-operative ischemia. On the other hand, these methods have acceptably high levels of sensitivity in detecting the brain ischemia. Furthermore, there is no method to detect the ischemic tolerance. Consequently, usage of any fashion of shunting should be justified under the above-mentioned circumstances. However, one study indicated that shunting might not be able to maintain local physiologic microcirculation.⁹⁾ Thus, it is also necessary to reduce the duration of the surgical procedure, as well.

CONCLUSION

Establishing a temporary femoral-carotid shunt is technically feasible. The shunt can refurbish the circulation of blood to the brain during carotid artery reconstruction in the hybrid procedure for aortic arch aneurysms.

REFERENCES

- 1) Kato N, Shimono T, Hirano T, Mizumoto T, Ishida M, Fujii H, et al. Aortic arch aneurysms: treatment with

- extraanatomical bypass and endovascular stent-grafting. *Cardiovasc Intervent Radiol* 2002; **25**: 419–22.
- 2) Diethrich EB, Ghazoul M, Wheatley GH 3rd, Alpern JB, Rodriguez-Lopez JA, Ramaiah VG. Great vessel transposition for antegrade delivery of the TAG endoprosthesis in the proximal aortic arch. *J Endovasc Ther* 2005; **12**: 583–7.
- 3) Chiesa R, Melissano G, Tshomba Y, Civilini E, Marone EM, Bertoglio L, et al. Ten years of endovascular aortic arch repair. *J Endovasc Ther* 2010; **17**: 1–11.
- 4) Roques F, Michel P, Goldstone AR, Nashef SA. Logistic or additive EuroSCORE for high-risk patients? *Eur Heart J* 2003; **24**: 881–2.
- 5) Edmonds HL, Ganzel BL, Austin EH. Cerebral oximetry for cardiac and vascular surgery. *Semin Cardiothorac Vasc Anesth* 2004; **8**: 147–66.
- 6) Hays RJ, Levinson SA, Wylie EJ. Intraoperative measurement of carotid back pressure as a guide to operative management for carotid endarterectomy. *Surgery* 1972; **72**: 953–60.
- 7) Minakawa M, Fukuda I, Yamauchi S, Watanabe K, Kawamura T, Taniguchi S, et al. Early and long-term outcome of total arch replacement using selective cerebral perfusion. *Ann Thorac Surg* 2010; **90**: 72–7.
- 8) Schönholz C, Ikonmidis JS, Hannegan C, Mendaro E. bailout percutaneous external shunt to restore carotid flow in a patient with acute type A aortic dissection and carotid occlusion. *J Endovasc Ther* 2008; **15**: 639–42.
- 9) Wilkinson JM, Rochester JR, Sivaguru A, Cameron IC, Fisher R, Beard JD. Middle cerebral artery blood velocity, embolisation, and neurological outcome during carotid endarterectomy: a prospective comparison of the Javid and the Pruitt-Inahara shunts. *Eur J Vasc Endovasc Surg* 1997; **14**: 399–402.

Case Report

A Case of Iatrogenic Subclavian Artery Injury Successfully Treated with Endovascular Procedures

Takuji Yamagami, MD, PhD,¹ Rika Yoshimatsu, MD, PhD,¹ Osamu Tanaka, MD, PhD,¹ Hiroshi Miura, MD,¹ Yutaka Kawahito, MD, PhD,² Katsuhiko Oka, MD,³ Hitoshi Yaku, MD, PhD,³ and Tsunehiko Nishimura, MD, PhD¹

We report a case of a life-threatening massive hemothorax caused by iatrogenic injury of the right subclavian artery. The patient was successfully treated with placement of a covered stent. During the procedure, occlusion balloon catheters rapidly controlled the massive bleeding.

Key words: hemorrhage, minimally invasive therapy, subclavian artery injury

INTRODUCTION

Although accidental arterial puncture may follow 1 out of 20 central venous catheterization attempts,¹⁾ this complication is often recognized before the catheter is introduced into the blood vessel due to pulsatile back-flow of oxygenated blood. Some patients experience massive bleeding from the insertion and immediate removal of a thin catheter into an artery. It was reported that the risk for serious complications after catheter removal increases with increases in the diameter of the catheter and length of time since catheter insertion.²⁾ Thus, in cases when the diameter of the access route is large, complications caused by accidental arterial catheterization are sometimes serious.

Recently, we encountered a case of a life-threatening

hemorrhage caused by inadvertent placement of a large vascular access catheter that damaged the right subclavian artery. For this case, we were successful in placing the covered stent on the area of injury, first by decreasing the blood flow with a balloon catheter.

CASE REPORT

A 23-year-old woman with systemic lupus erythematosus and severe liver dysfunction had a bedside plasma exchange, by the insertion of an 11-F double lumen Shalton catheter into the right jugular vein. The chest roentgenogram taken just after the catheter implantation led us to suspect misplacement of the catheter (**Fig. 1**). Enhanced chest computed tomography (CT) showed a right pneumohemothorax with the catheter running outside of the right jugular vein, close to the right subclavian artery with its tip located in the right pleural cavity. Before the procedure, the patient's hemoglobin had been 10.3 g/dl, but just after the enhanced CT, it had decreased to 7.8 g/dl. At that time, the blood pressure was 112/75 mmHg and the heart rate was 58 beats/min. After the patient had given written informed consent, we began endovascular treatment with local anesthesia to stop the bleeding.

First, we inserted a 4-F catheter from the left femoral artery to the right subclavian artery. Since the right subclavian arteriogram showed no extravasations, we slowly withdrew the Shalton catheter. Then, the blood pressure rapidly decreased to 82/21 mmHg, and the heart rate was

¹Department of Radiology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Kyoto, Japan

²Department of Inflammation and Immunology, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Kyoto, Japan

³Division of Cardiovascular Surgery, Department of Surgery, Graduate School of Medical Science, Kyoto Prefectural University of Medicine, Kyoto, Kyoto, Japan

Received: November 25, 2010; Accepted: January 4, 2011

Corresponding author: Takuji Yamagami, MD, PhD. Graduate School of Medical Science, Kyoto Prefectural University of Medicine, 465 Kajii-cho, Kawaramachi-Hirokoji, Kamigyo-ku, Kyoto, Kyoto 602-8566, Japan

Tel: +81-75-251-5620, Fax: +81-75-251-5840

E-mail: yamagami@koto.kpu-m.ac.jp

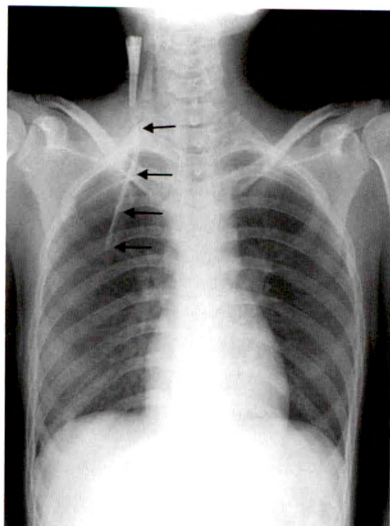


Fig. 1 Chest roentgenogram of misplaced Shaldon catheter (arrows) after catheter implantation.



Fig. 2 Right subclavian arteriography of rapid and continuous extravasations from the right subclavian artery (arrows) after withdrawal of Shaldon catheter.

120 beats/min. The patient had temporary loss of consciousness. Then we took a right subclavian arteriograph, which revealed rapid and continuous extravasations from the right subclavian artery (**Fig. 2**). Second, after inflating the 5-F balloon catheter (9 mm diameter) at the point to decrease the bleeding, we removed the 4-F catheter. We then advanced a guide wire to the right brachial artery through the 5-F balloon catheter. Third, we advanced an 18-gauge intravenous catheter (Surflo; Terumo, Tokyo, Japan) at the guide wire and advanced the 5-F sheath introducer into the right brachial artery. Then, we advanced a 5-F balloon catheter (11 mm diameter) from the right brachial artery to the bleeding point and inflated the 5-F balloon to decrease the bleeding after withdrawal of the 5-F balloon catheter (**Fig. 3**). Fourth, we exchanged the left femoral artery sheath with a 9-F sheath introducer and a self-expandable metallic covered stent (8 mm diameter) and then inserted a 5-cm long stent (Niti-S ComVi stent; Taewoong Medical, Gimpoo, Korea). Before deployment, the stent was advanced to the point where the brachial balloon would be positioned. The brachial balloon catheter was deflated and pulled back to the distal part of the right subclavian artery. In the next instant, we placed the covered stent in the right subclavian artery to cover the bleeding point. After the stent placement, the hemorrhage was no longer visible in the right subclavian arteriography (**Fig. 4**). The stent successfully closed the source of bleeding of the right vertebral artery; however, the left vertebral arteriogram clearly

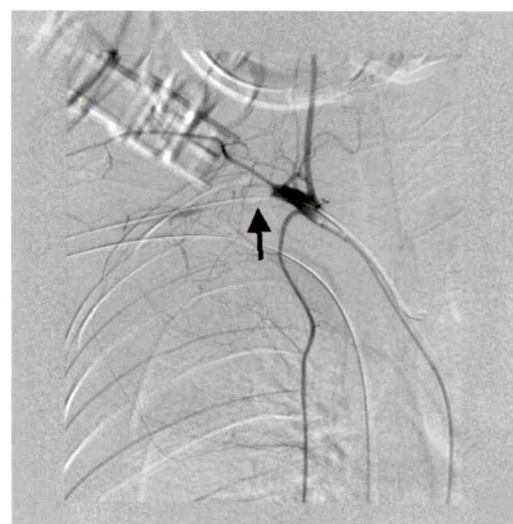


Fig. 3 Right subclavian arteriography of inflated balloon catheter (arrow) advancing from the brachial artery with no extravasations.

showed centripetal flow in the entire right vertebral artery. After stent placement, we drained 2 liters of bloody pleural fluid with a chest tube. The entire procedure took approximately 3 hours.

The anemia resolved after stent placement and infusion of 1300 mL of red blood cell concentrate. Plasma exchange was performed after re-insertion of the Shaldon catheter. Discharge of bloody pleural fluid from the chest tube immediately decreased and finally disappeared. The chest tube was removed 9 days after stent placement. Therapies

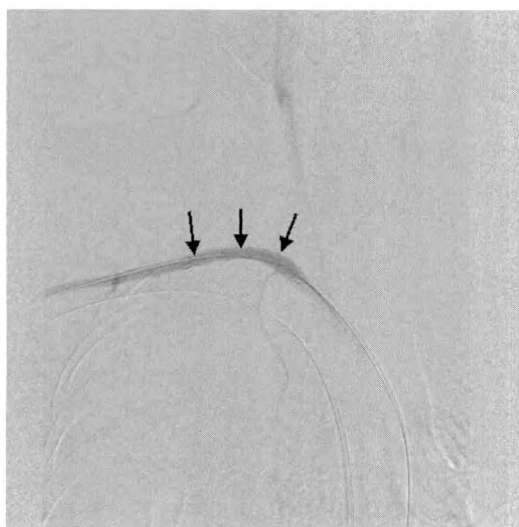


Fig. 4 Right subclavian arteriography of the stent (arrows) stopping the extravasations.

for systemic lupus erythematosus were resumed. More than 5 months after stent placement, the patient did not experience any hemorrhaging from the right subclavian artery, and covering the origin of the right vertebral artery did not cause any neurological symptoms.

DISCUSSION

There is widespread use of a central venous catheter to provide venous access for nutritional support or management of peri-operative fluids. Central venous access procedures are associated with inadvertent arterial puncture in up to 5% of cases.¹⁾ Because this complication is often recognized before the insertion of the catheter into the blood vessel, inadvertent arterial catheterization is much less common.

Treatment strategies after inadvertent arterial catheterization include local compression, open surgical treatment with direct arterial repair and percutaneous endovascular treatment.²⁾ When hemostasis is not obtained by local compression,^{2, 3)} surgical treatment or percutaneous endovascular treatment should be chosen.^{2, 3)} Surgical treatment is usually safe; however, it can add significant morbidity as patients undergoing placement of a central venous catheter are often seriously ill and open repair can be complex, requiring general anesthesia and perhaps sternotomy.²⁾ On the other hand, less invasive percutaneous endovascular treatment of the inadvertent catheterization of the carotid or subclavian artery can be performed while the patient is under local anesthesia. In such percu-

taneous endovascular treatments, there are two options: use of a percutaneous closure device or a stent graft.²⁻⁵⁾

In this study, while the patient was under local anesthesia, we successfully deployed a 5-cm Niti-S ComVi stent to stop a massive hemorrhage caused by inadvertent catheterization of a wide vascular access (11-F) to the subclavian artery. This stent is a self-expandable Nitinol covered by a 4-cm-long membrane of polytetrafluoroethylene, 0.5 cm uncovered at each end. For stoppage of massive bleeding, it is extremely useful to place the balloon catheter close to the bleeding area during withdrawal of the inadvertently placed catheter and until insertion of the stent. Even when an evident extravasation is not viewable in scans, the inadvertently placed catheter may be compressing the area and stopping the bleeding^{6, 7)}; thus, the catheter should not be withdrawn until preparations are ready for carrying out the procedure in the angiography room. Above all, we recommend ultrasonographic- and fluoroscopic-guidance in the angiography room for the safe insertion of a vascular access catheter, especially for those with large diameters. Insertion at the bedside should be avoided.

REFERENCES

- 1) Eisen LA, Narasimhan M, Berger JS, Mayo PH, Rosen MJ, Schneider RF. Mechanical complications of central venous catheters. *J Intensive Care Med* 2006; **21**: 40–6.
- 2) Pikwer A, Acosta S, Kolbel T, Malina M, Sonesson B, Akeson J. Management of inadvertent arterial catheterization associated with central venous access procedures. *Eur J Vasc Endovasc Surg* 2009; **38**: 707–14.
- 3) Cayne NS, Berland TL, Rockman CB, Manadonado TS, Adelman MA, Jacobowitz GR, et al. Experience and technique for the endovascular management of iatrogenic subclavian injury. *Ann Vasc Surg* 2010; **24**: 44–7.
- 4) Shetty SV, Kwolek CJ, Garasic JM. Percutaneous closure after inadvertent subclavian artery cannulation. *Catheter Cardiovasc Interv* 2007; **69**: 1050–2.
- 5) Midorikawa H, Kannno M, Ishikawa K, Takano T, Ono T, Morishima S. Endovascular repair of a Kommerell's diverticulum and aneurismal right-sided aortic arch: a case report. *Ann Vasc Dis* 2009; **2**: 54–7.
- 6) Cil BE, Canyigit M, Penyircioglu B, Harizolan T, Carkaci S, Cekirge S, et al. Subcutaneous venous port implantation in adult patients: a single center experience. *Diagn Interv Radiol* 2006; **12**: 93–8.
- 7) Dede D, Akmangit I, Yildirim ZN, Sanverdi E, Sayin B. Ultrasonography and fluoroscopy-guided insertion of chest ports. *Eur J Surg Oncol* 2008; **34**: 1340–3.

» Case Report «

Mycotic Abdominal Aneurysm Caused by *Campylobacter Fetus*: A Case Report for Surgical Management

Yukihiro Noda, MD,¹ Ko-ichiro Sawada, MD,¹ Syu-hei Yoshida, MD,¹ Satoru Nishida, MD,¹
Shinichiro Yamamoto, MD,¹ Yuji Otake, MD,² and Go Watanabe, MD²

We report a rare case of mycotic abdominal aortic aneurysm associated with *Campylobacter fetus*. A 72-year-old male admitted to the hospital because of pain in the right lower quadrant with pyrexia. The enhanced abdominal computed tomography (CT) examination showed abdominal aortic aneurysm (AAA) measuring 50 mm in maximum diameter and a high-density area of soft tissue density from the right lateral wall to the anterior wall of the aorta. However, since the patient showed no significant signs of deferescence after antibiotics administration, so we performed emergency surgery on the patient based on the diagnosis of impending rupture of mycotic AAA. The aneurysm was resected in situ reconstruction using a bifurcated albumin-coated knitted Dacron graft was performed. The cultures of blood and aneurysmal wall grew *Campylobacter fetus*, allowing early diagnosis and appropriate surgical management in this case, and the patient is making satisfactory progress. This is the fifth report of mycotic AAA characterizing culture positive for *Campylobacter fetus* in blood and tissue culture of the aortic aneurysm wall.

Key words: mycotic abdominal aneurysm, *Campylobacter fetus*, vascular surgery

INTRODUCTION

Campylobacter fetus infection associated with endocarditis and meningitis and a decline in the patient's general condition is becoming more prevalent in patients.^{1, 2)} With mycotic abdominal aortic aneurysm (AAA) involvement, *Campylobacter fetus* is difficult to diagnosis early, and there is a high risk of aneurysm rupture due to rapid dilation. This is one of several case reports on a patient with mycotic AAA positive for *Campylobacter fetus* in the blood and tissue cultures of aneurysm wall samples.

¹Department of Cardiovascular Surgery, Fukui Prefectural Hospital, Fukui, Fukui, Japan

²Department of General and Cardiothoracic Surgery, Kanazawa University Graduate School of Medical Science, Kanazawa, Ishikawa, Japan

Received: June 29, 2010; Accepted: January 11, 2011
Corresponding author: Yukihiro Noda, MD, Department of Cardiovascular Surgery, Fukui Prefectural Hospital, 2-8-1 Yotsui, Fukui, Fukui 910-8526, Japan
Tel: +81-776-54-5151, Fax: +81-776-58-57-2945
E-mail: noyu@mvp.biglobe.ne.jp

CASE REPORT

A 72-year-old man with hypertension and no history of overseas voyage or animal contact was admitted to the hospital for surgical treatment. The patient developed symptoms of right lower quadrant abdominal pain, vomitus and fever of 38°C after the admission. Pulsating abdominal mass was not palpable, while tenderness in the right lower quadrant without muscular defense was present. There was hyperinflammatory reaction indicated by white blood cell count of 10,300/μl (Neutrophil 76.5%) and C-reactive protein (CRP), 1.6 mg/dL. Liver function, renal function, and electrolytes were all normal. We performed an enhanced abdominal computed tomography (CT) examination of the patient for suspected acute appendicitis; however, there were no swollen appendix, just findings of AAA with 50 mm in maximum diameter and a deposition pattern of high-density area of soft tissue from the right lateral wall to the anterior wall of the aorta instead (**Fig. 1**). Blood cultures were positive for *Campylobacter fetus*.

Clinical findings and CT images revealed an impending rupture of mycotic AAA, and the patient underwent

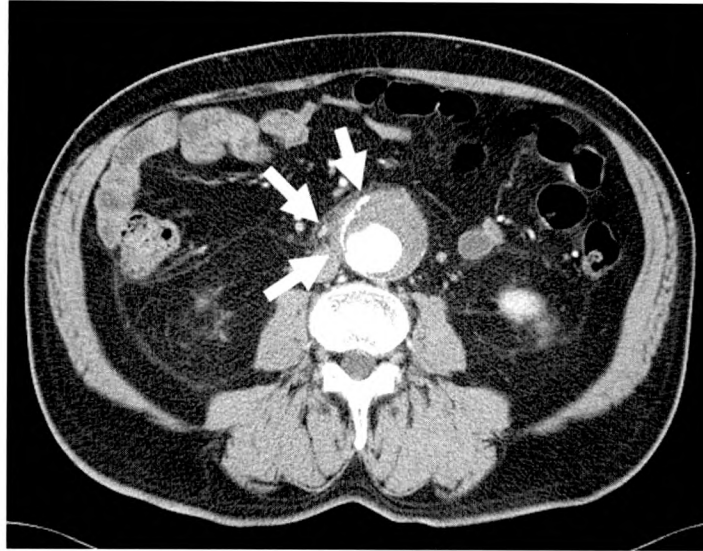


Fig. 1 A deposition pattern of high-density area of soft tissue density from the right lateral wall to the anterior wall of the aorta (arrow).

surgery in which we found infrarenal AAA with a 50-mm maximum diameter, a hyperinflammatory state, and hypertrophy of the adventitia of the anterior and right lateral wall. The entire retroperitoneum was edematous. Intraoperative findings were compatible with the preoperative CT examination. The Intramural thrombus was removed carefully, and the aneurysm wall was resected. Following an adequate washing procedure with a combination of povidone iodine solution and physiological saline, we replaced by a Y-shaped woven Dacron graft (16 × 8mm, Hemashield) without Omental wrapping, since there was no evidence of abscess formation.

Postoperative germ culture of the resected aneurysm wall was positive for *Campylobacter fetus*. The pathological findings showed extensive calcification and hypertrophy of tunica intima due to atheroma formation with cholesterol slits. The elastic lamina in the media was damaged and eventually the fibrous lesions extended to the tunica adventitia. Although the adventitia had hemorrhaged, with infiltration of neutrophils and lymphocytes, there was no evidence of abscess. Neither bacteria or mold was detected. All these findings suggest a mycotic AAA caused by *Campylobacter fetus* infection of the atherosclerotic aorta.

The patient was treated with Meropenem 1.5 mg/day for 14 days after the surgery (co-administrated with immunoglobulin in the first 3 days), replaced by Ciprofloxacin hydrochloride (CPFX) 600 mg/day for the next 17 days. The patient began Levofloxacin (LVFX) treat-

ment on day 30 after the surgery and was discharged on day 38. At one year follow-up, the patient had a negative CT scan and was symptom-free.

DISCUSSION

The incidence of mycotic AAA is relatively rare, between 1% and 3% of patients with AAA. Since the disease is characterized by a rapid decline in the patient's condition, the risk of aneurysmal rupture is estimated to be between 50% and 80%.³⁻⁵⁾

According to the clinical criteria introduced by Müller et al., mycotic aneurysm can be diagnosed when there is 1) a positive aortic wall germ culture (including surrounding tissue or contents of the intra aneurysm, for example, the intramural thrombus) and clinical signs or 2) a negative germ culture plus rupture of AAA, unusual clinical signs during surgery (infection) or ongoing antibiotic treatment.⁴⁾ Our diagnosis of mycotic AAA was based on criteria 1) because we were not able to define the route of infection in the patient (In spite of the careful anamnesis). However, a preoperative blood culture tested positive for *Campylobacter fetus*. Therefore, we concluded that the progress of infection in the aortic wall that began with bacteremia was the cause of the mycotic AAA. The patient did have two out of three of the symptoms of mycotic AAA: pyrexia and abdominal pain, though he did not have the third, an abdominal mass. In the image diagnostics, the CT scan is highly effective in

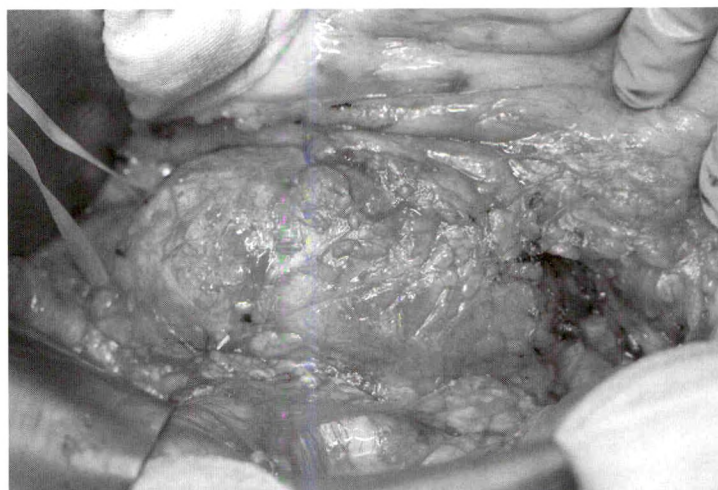


Fig. 2 Intraoperative finding of aneurysm. Infrarenal AAA, hyperinflammatory reaction and hypertrophy of the adventitia of the anterior and right lateral wall was found. The entire retroperitoneum was edematous.
AAA, abdominal aortic aneurysm

evaluation of the time-dependent changes in aneurysmal expansion. Macedo has reported that relatively high number of cases which shows saccular aneurysm with lobular lumen is indicative of mycotic aneurysm.⁷⁾ In addition, the increase of peri-aortic fat density and presence of edema the aorta are significant findings that should be carefully evaluated. The former is also considered being a key factor in the estimation of changes in the retroperitoneum caused by the inflammatory reaction. Our case presented with these findings, which eventually led to the early diagnosis of impending rupture of mycotic AAA, and immediate surgical treatment to prevent the rupture of the aneurysm.

The pathogenic bacteria complicating mycotic AAA are usually salmonella, staphylococcus or streptococcus; however, *Campylobacter fetus* has also been reported to complicate mycotic AAA.⁶⁻¹³⁾

Campylobacter fetus, a helical, microaerophilic, Gram-negative rod, is reported to cause miscarriage in livestock, especially in cattle and sheep.^{6, 7)} In humans, it is associated with a decline in the physical condition, eventually leading to endocarditis and meningitis.^{1, 2)} We have found 15 cases of *Campylobacter fetus* infection inducing mycotic AAA (13, male; 2, female; average age, 64.4 years; range, 45–84 years).⁸⁻¹³⁾ Subjective symptoms were 10 cases of pyrexia (66.6%), 6 cases of abdominal pain (40%), 6 cases of diarrhea (40%), 3 cases of nausea (20%), 3 cases of low back pain (20%), and 1 case of weight loss and anorexia (6.7%). In treatments, 8 cases for

anatomic reconstruction and 4 cases for extra-anatomical bypass had been performed. As the result, 4 cases died in aneurysm rupture and 3 cases was not applied surgical treatment among them. There were differences in the period of antibiotics administration between each case ranged from 7 days to 7 months.

Normally extra-anatomical bypass or anatomic reconstruction, such as prosthetic graft replacement, is applied to mycotic infrarenal AAA. While extra-anatomical bypass was commonly performed in the past, anatomic reconstruction, resection of aneurysm wall, and covering of the prosthetic graft with omental wrapping have been introduced with favorable outcomes.^{14, 15)} In our case, we selected in-situ prosthetic graft replacement because pus discharge was not observed during surgery. We considered omental wrapping; however, the omentum was severe atrophied from the inflammation, and we could not perform the procedure. We also removed the intramural thrombus carefully and washed the area with warm physiological saline to prevent infection.

Even though there is no standard-of-care for the term of prophylatic use of oral antibiotics, treatment is often continued for several months after any evidence of infection. However, we usually stop antibiotic treatment when the biochemical test for blood inflammatory response markers is negative. The patient tested negative for CRP after 10 weeks of antibiotic therapy; thus, the treatment was stopped.

For mycotic AAA, it is usually advisable to treat the

bacterial infection with antibiotics first, as in this case, and consider surgery when the infection is under control.^{3,4)} However, surgery is indicated in patients with a rapidly expanding aneurysm or in non-responders to antibiotics.

In this case, since the follow-up CT scan revealed a dense, fatty area with exacerbation of the adjacent soft-tissue mass, we operated to prevent an aneurysm rupture.

One year after surgery, the patient has been returning for regular check-ups with no evidence of the disease, though we will continue long-term follow-up to monitor any recurrence of local or systemic infection.

REFERENCES

- 1) Miki K, Maekura R, Hiraga T, Hirotani A, Hashimoto H, Kitada S, et al. Infective tricuspid valve endocarditis with pulmonary emboli caused by *Campylobacter fetus* after tooth extraction. *Intern Med* 2005; **44**: 1055–9.
- 2) Herve J, Aissa N, Legrand P, Sorkine M, Calmette MJ, Santin A, et al. *Campylobacter fetus* meningitis in a diabetic adult cured by imipenem. *Eur J Clin Microbiol Infect Dis* 2004; **23**: 722–4.
- 3) Alonso M, Caeiro S, Cachaldora J, Segura R. Infected abdominal aortic aneurysm in situ replacement with cryopreserved arterial homograft. *J Cardiovasc Surg* 1997; **38**: 371–5.
- 4) Müller BT, Wegener OR, Grabitz K, Pillny M, Thomas L, Sandmann W. Mycotic aneurysms of the thoracic and abdominal aorta and iliac arteries: Experience with anatomic and extra-anatomic repair in 33 cases. *J Vasc Surg* 2001; **33**: 106–13.
- 5) Oderich GS, Panneton JM, Bower TC, Cherry KJ Jr, Rowland CM, Noel AA. Infected aortic aneurysms: Aggressive presentation, complicated early outcome, but durable results. *J Vasc Surg* 2001; **34**: 900–8.
- 6) Hsu RB, Chen RJ, Wang SS, Chu SH. Infected aortic aneurysms: Clinical outcome and risk factor analysis. *J Vasc Surg* 2004; **40**: 30–5.
- 7) Macedo TA, Stanson AW, Oderich GS, Johnson CM, Panneton JM, Tie ML. Infected aortic aneurysms: Imaging findings. *Radiology* 2004; **231**: 250–7.
- 8) Marty AT, Webb TA, Stubbs KG, Penkava RR. Inflammatory abdominal aortic aneurysm infected by *campylobacter fetus*. *JAMA* 1983; **249**: 1190–2.
- 9) Anolik JR, Mildvan D, Winter JW, Puttlitz D, Rubenstein S, Lozman H. Mycotic aortic aneurysm. *Arch Intern Med* 1983; **143**: 609–10.
- 10) Jacobs J, Van Lierde J, Nevelsteen A, Vermeylen J, Verbist L. *Campylobacter fetus* subspecies *fetus* infection of an abdominal aneurysm. *Acta Clini Belg* 1989; **44**: 123–8.
- 11) Kato R, Ohta T, Kazui H, Kondo M, Naiki K, Tsuchioka H. *Campylobacter fetus* infection of abdominal aortic aneurysm. *J Cardiovasc Surg* 1990; **31**: 756–9.
- 12) Kato R, Ohta T, Kazui H, Kondo M, Naiki K, Tsuchioka H. Infected abdominal aneurysm caused by *campylobacter fetus* subspecies *fetus*: report of a case. *Surg Today* 1998; **28**: 661–4.
- 13) Tran JK, de Virgilio C. Management of an abdominal aortic aneurysm infected with *campylobacter fetus*: a case report. *Ann Vasc Surg* 2007; **21**: 137–42.
- 14) Kuniyoshi Y, Koja K, Miyagi K, Uezu T, Yamashiro S, Arakaki K. Graft for mycotic thoracic aortic aneurysm: omental wrapping to prevent infection. *Asian Cardiovasc Thorac Ann* 2005; **13**: 11–6.
- 15) Park SJ, Kim MN, Kwon TW. Infected abdominal aortic aneurysm caused by *Brucella abortus*: a case report. *J Vasc Surg* 2007; **46**: 1277–9.

» Case Report «

Successful Surgical Treatment of Right Subclavian Artery Aneurysm with a Hypoplastic Left Vertebral Artery Using Temporary Cerebral Perfusion to Prevent Cerebral Ischemia

Hiroshi Ito, MD, PhD, Hiroshi Kurazumi, MD, Kensuke Sakata, MD, and Yurio Koabayashi, MD

A 71-year-old man had a right subclavian artery aneurysm (dimension, 30 × 38 mm) that was adjacent to the right common carotid artery and exceedingly close to the right vertebral artery. The patient had a marked hypoplastic left vertebral artery, dominant right vertebral artery, and an incompletely formed and underdeveloped circle of Willis in the skull. While performing a median sternotomy and supraclavicular incision during the operation, we used temporal shunting for the cerebral perfusion. The subclavian artery aneurysm was resected, and a 10-mm diameter woven Dacron graft was used for reconstructing the subclavian artery. The postoperative course was uneventful, and the patient was discharged from the hospital 18 days after surgery. Temporal shunting for maintaining cerebral perfusion was useful in preventing cerebral ischemia, and the median sternotomy plus supraclavicular incision approach afforded an unobstructed view of the surgical field.

Key words: subclavian artery aneurysm, cerebral artery perfusion, hypoplastic vertebral artery

INTRODUCTION

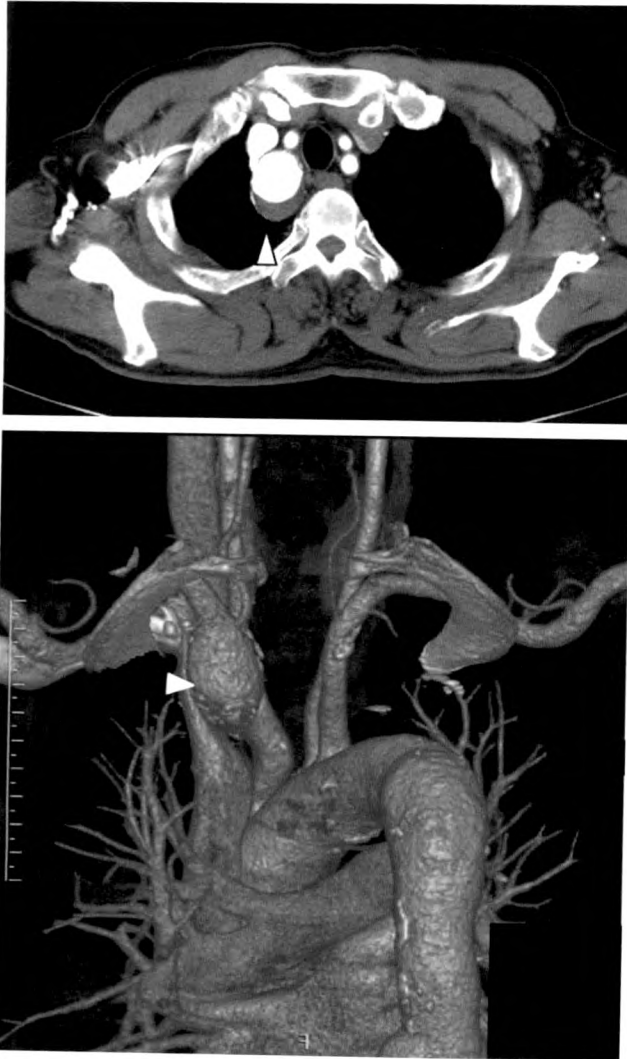
Subclavian artery aneurysm is a rare disorder that only accounts for 0.13%–2.8% of all peripheral aneurysms that affect the limbs.^{1,2)} Surgery is the method of choice for treating this aneurysm. However, cerebral protection by means of temporary perfusion might become inevitable in cases where the carotid and vertebral arteries are affected by the aneurysm. We present a case of surgical treatment of subclavian artery aneurysm using temporary cerebral perfusion to prevent cerebral ischemia.

Department of Cardiovascular Surgery, Saiseikai Shimonoseki General Hospital, Shimonoseki, Yamaguchi, Japan

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Corresponding author: Hiroshi Ito, MD, PhD. Department of Cardiovascular Surgery, Saiseikai Shimonoseki General Hospital, 8-5-1 Yasuoka, Shimonoseki, Yamaguchi 759-6603, Japan
Tel: +81-83-262-2300, Fax: +81-83-262-2301
E-mail: h-ito@simo.saiseikai.or.jp

CASE

A 71-year-old man, presenting with severe back pain, was diagnosed with Stanford type B acute aortic dissection. He was under medical treatment for a period of 11 months before surgery. Computed tomographic (CT) examination conducted during this period revealed a right subclavian artery aneurysm that was 30 mm in diameter, and over 10 months, its size had gradually increased; thus, the patient was referred to the Saiseikai Shimonoseki General Hospital. CT scanning revealed a right subclavian artery aneurysm (dimension, 30 × 38 mm) located adjacent to the right common carotid artery and extremely close to the right vertebral artery (**Fig. 1A** and **1B**). Magnetic resonance angiography (MRA) of the head and neck revealed a marked hypoplastic left vertebral artery and a dominant right vertebral artery (**Fig. 2A**). The circle of Willis was incompletely formed and underdeveloped (**Fig. 2B**). From all these results, the neurosurgeon concluded that an occlusion test of the right vertebral artery was too risky to perform because ischemia might develop in the basal region of the right verte-

**Fig. 1**

- A:** Computed tomographic analysis showing a right subclavian artery aneurysm, 30 × 38 mm (indicated by arrowhead).
- B:** Right vertebral artery branched at the periphery of the aneurysm (indicated by arrowhead).

**Fig. 2**

- A:** Magnetic resonance angiography showing hypoplasia of the left vertebral artery (indicated by arrowhead).
- B:** Poor collateral circulation through the circle of Willis.

bral artery during reconstruction of the right subclavian artery. Therefore, we could not perform the occlusion test, and instead we used a temporal shunt for the cerebral perfusion while performing the surgery.

Median sternotomy and supraclavicular incision were performed. The brachiocephalic artery, right common carotid artery, right subclavian artery, and right vertebral artery were identified. After systemic heparinization by the administration of 7000 U heparin, a Y-shape cardioplegia needle, which can deliver approximately 300 ml/min of blood flow, was inserted at the level of the

ascending aorta. Brachiocephalic artery and distal site of subclavian artery were clamped during anastomosis, and perfusion to the right common carotid artery and the right vertebral artery was performed using cerebral perfusion tubes (12 Fr and 8 Fr, SUMITOMO BAKELITE Co., Ltd. Tokyo) (**Fig. 3**). A 10-mm in diameter InterGard woven graft (Inter Vascular, Montvale) was used for reconstructing the subclavian artery (**Fig. 4**). Cerebral blood flow was monitored by near-infrared spectroscopy, and no sign of ischemia was observed. The postoperative course was uneventful, and he was discharged from the

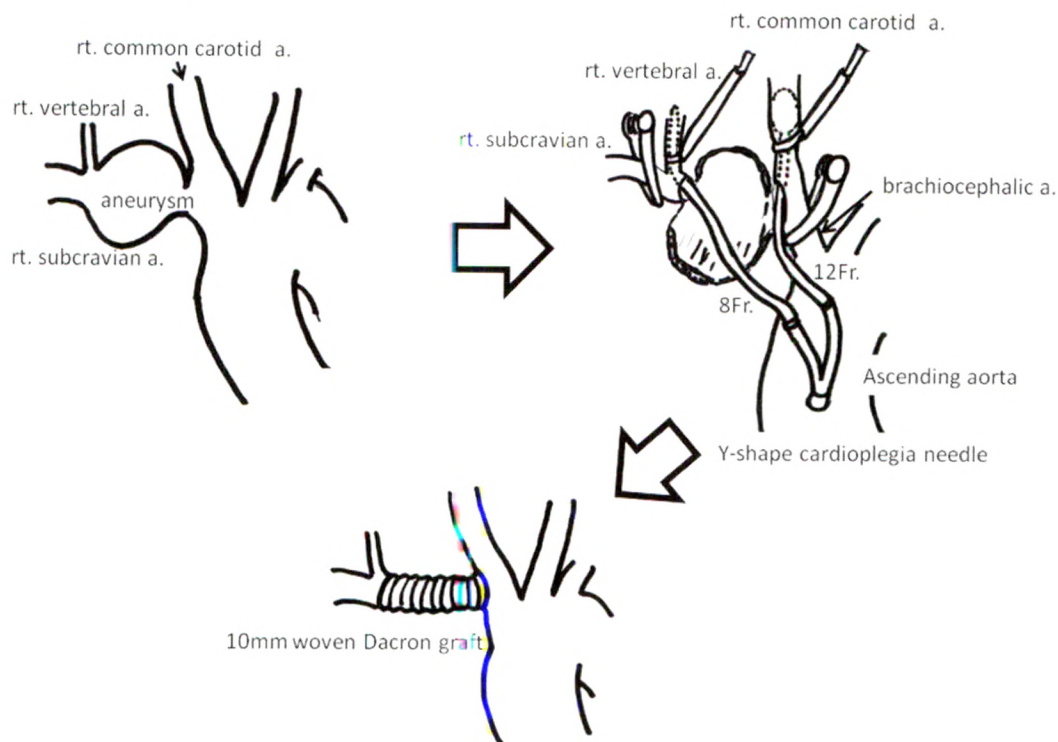


Fig. 3 Brachiocephalic artery and distal site of right subclavian artery were clamped during anastomosis. A y-shape cardioplegia needle was inserted at the ascending aorta, and right common carotid artery and vertebral artery perfusion was performed.

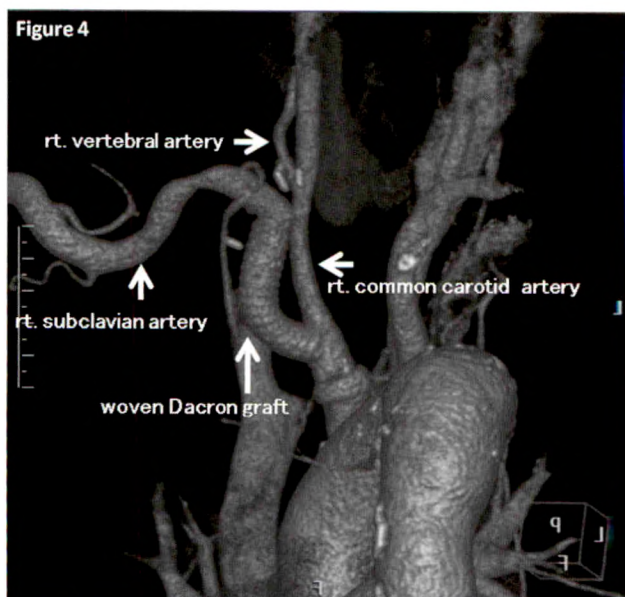


Fig. 4 Reconstruction of the right subclavian artery with a 10-mm woven Dacron graft.

hospital 18 days after surgery. The pathological findings revealed an atherosclerotic aneurysm.

DISCUSSION

Subclavian artery aneurysm is relatively rare, and it accounts for only 0.13%–2.8% of all the peripheral artery aneurysms.^{1, 2)} Injuries or infections such as syphilis and tuberculosis are considered to be the main causes of aneurysm; however, Dougherty reported that 60% of subclavian artery aneurysms are atherosclerotic aneurysms.³⁾ It has also been reported that 30%–50% of patients with subclavian artery aneurysm also have other peripheral artery aneurysms, such as iliac artery aneurysm.⁴⁾ Other causes of subclavian artery aneurysm are aortic inflammation, Behcet's disease, Marfan syndrome, Ehlers-Danlos syndrome, and thoracic outlet syndrome.^{3–7)} The patient had no history of trauma or infection, and the pathological findings suggested the presence of an atherosclerotic aneurysm.

Most patients with atherosclerotic aneurysm are asymptomatic, though the condition is occasionally diag-

nosed from chest X-ray or CT scan images. Neurological symptoms such as upper limb pain or chest pain, movement disorder, hoarseness, paralysis, sensory disorder, and Horner's syndrome are often observed in these patients.⁴⁾ Thromboembolisms in the upper limb or vertebral arteries and the common carotid artery have also been reported.⁴⁾

Surgical intervention is the method of choice for treating this aneurysm. The approach used for treating the aneurysm differs according to its location. When it is located in the extrathoracic region, a supra-infraclavicular incision approach is chosen.⁴⁾ Left posterolateral thoracotomy is used when the aneurysm is located in the left thoracic cavity. Supraclavicular incision plus median sternotomy, partial sternotomy, or trapdoor thoracotomy are usually used for approaching right intrathoracic subclavian artery aneurysms.⁴⁾ In the present case, we used a supraclavicular incision plus median sternotomy approach. The reasons for selecting this approach are as follows: 1) the aneurysm was located in the intrathoracic space and close to the common carotid and vertebral arteries, and 2) the right vertebral artery was dominant and the left vertebral artery was hypoplastic; in addition, the circle of Willis was poorly connected to the basal artery. To avoid cerebral ischemia, we perform temporal perfusion to the right common carotid and vertebral arteries during the reconstruction. The supraclavicular incision plus median sternotomy approach also provided an unobstructed field of view and afforded easy establishment of perfusion from the ascending aorta to the carotid and vertebral arteries. Inflow of the shunt was used at the ascending aorta in this case. Cannulation of the ascending aorta may cause cerebral infarction; however, the ascending aorta in this case did not demonstrate atherosclerosis by preoperative CT or echocardiogram. Then we thought the risk of cerebral infarction was low in this case. If the ascending aorta had severe atherosclerosis, cannulation site was considered to be the femoral artery or left subclavian artery. From our experience, we recommend this procedure.

The operative procedure usually involves interposition of the artificial graft or end-to-end anastomosis. However, if the aneurysm is located just above the aortic arch, total arch replacement might have to be performed.⁸⁾

More recently, endovascular treatment by stent grafting of the subclavian arteries has also been reported; it also promises to be a less invasive and a low-risk treatment as compared to surgery.⁹⁻¹¹⁾ However, applying stent grafts to the sites of aneurysm in the vertebral or carotid artery is difficult.

REFERENCES

- 1) Crawford ES, DeBakey ME, Cooley DA. Surgical considerations of peripheral arterial aneurysms; analysis of one hundred seven cases. *AMA Arch Surg* 1959; **78**: 226-38.
- 2) Dent TL, Lindenauer SM, Ernst CB, Fry WJ. Multiple arteriosclerotic arterial aneurysms. *Arch Surg* 1972; **105**: 338-44.
- 3) Dougherty MJ, Calligaro KD, Savarese RP, DeLaurentis DA. Atherosclerotic aneurysm of the intrathoracic subclavian artery: a case report and review of the literature. *J Vasc Surg* 1995; **21**: 521-9.
- 4) Clagett GP. Upper extremity aneurysm. In: Rutherford RB, editor. *Vascular Surgery*. 5th edition. Philadelphia: W.B. Saunders, 2000: 1356-69.
- 5) Pairolero PC, Walls JT, Payne WS, Hollier LH, Fairbairn JF 2nd. Subclavian-axillary artery aneurysms. *Surgery* 1981; **90**: 757-63.
- 6) Applebaum RE, Caniano DA, Sun CC, Azizkhan RA, Queral LA. Synchronous left subclavian and axillary artery aneurysms associated with melorheostosis. *Surgery* 1986; **99**: 249-53.
- 7) McCollum CH, Da Gama AD, Noon GP, DeBakey ME. Aneurysm of the subclavian artery. *J Cardiovasc Surg (Torino)* 1979; **20**: 159-64.
- 8) Nakamura K, Murakami M, Asai T, Saito Y, Suda Y, Yamaguchi H. Distal arch replacement for intrathoracic left subclavian artery aneurysm in a 68-year old man. *Jpn J Cardiovasc Surg* 2007; **36**: 218-20. (in Japanese)
- 9) Sivamurthy N, Eichler C, Schneider DB. Endovascular exclusion of subclavian artery pseudoaneurysm. *Vascular* 2006; **14**: 231-5.
- 10) Schönholz CJ, Uflacker R, De Gregorio MA, Parodi JC. Stent-graft treatment of trauma to the supra-aortic arteries. A review. *J Cardiovasc Surg (Torino)* 2007; **48**: 537-49.
- 11) Chambers CM, Curci JA. Treatment of nonaortic aneurysms in the endograft era: aneurysms of the innominate and subclavian arteries. *Semin Vasc Surg* 2005; **18**: 184-90.

» **Short Communication** «

A Case of Effective Cerebrospinal Fluid Drainage for Paraplegia Caused by Acute Aortic Dissection

Yukihiro Hayatsu, MD, Koichi Nagaya, MD, Kei Sakuma, MD, and Susumu Nagamine, MD

A 65-year-old man with sudden back pain was transferred to our hospital by ambulance, who also complained of sensory and motor disorder of bilateral legs on arrival. The neurological disorder was gradually aggravated and paraplegia below the level of Th10 was manifested. Computed tomography demonstrated DeBakey IIIb acute aortic dissection; therefore, the paraplegia was thought to be due to spinal cord ischemia caused by the acute aortic dissection. Emergent cerebrospinal fluid drainage was performed, and it was very effective for the relief from paraplegia. The hospital course after the drainage was uneventful and he was discharged on the 39th day after the onset of symptoms.

Key words: acute aortic dissection, paraplegia, cerebrospinal fluid drainage

CASE

A 65-year-old man with sudden and severe back pain was transferred to our hospital. On arrival, several signs of paraplegia below the level of Th10 were observed, and it was gradually aggravated. Other physical examinations and laboratory data were normal except for slight inflammatory changes. As acute aortic dissection was suspected, an emergent plain computed tomography (CT) was performed because of an allergy to contrast medium. The CT (**Fig. 1**) showed DeBakey type IIIb acute aortic dissection. Physical examinations and the CT suggested no other visceral malperfusions without the paraplegia. It was thought to be by spinal cord ischemia due to acute aortic dissection, and we performed only cerebrospinal fluid (CSF) drainage immediately for the relief from the paraplegia. A catheter (Shirasukon L-P shunt type K[®]; KANEKA MEDIX CORP) for CSF drainage was intro-

duced into intervertebral space between 4th to 5th lumbar vertebra in which the pressure of CSF was about 25 mmHg. CSF, which was drained vigorously, and soon after the drainage, the paraplegia was dramatically improved. Continuous CSF drainage was started about 4 hours after his onset and continued for 85 hours. Muscle strength in his legs improved from grade 1/5 to grade 4/5 when he left ICU. The catheter was removed on the 4th day after initiation, and 250 mL of CSF was drained for 85 hours. The clinical course of the patient in the hospital was uneventful. The CT on 29th hospital day showed a true aortic aneurysm at distal aortic arch and the thrombosed dissecting aneurysm extended from distal aortic arch to the level of diaphragm (**Fig. 2**). The Adamkiewicz artery was identified as arising from left 9th intercostal artery penetrating the thrombosed aortic aneurysm (**Fig. 3**). The patient was discharged on the 39th day after his admission and is under close observation at our outpatient clinic.

COMMENT

Paraplegia is a rare but devastating complication associated with acute aortic dissection. It is reported to occur in 4% of all patients.^{1,2)} A third of the ventral spinal cord was perfused by the anterior spinal artery, and two thirds of the dorsal spinal cord was perfused by the posterior spinal artery. Poor fluctuation continuity and segmental

Department of Cardiovascular Surgery, Iwate Prefectural Central Hospital, Morioka, Iwate, Japan

Received: July 23, 2010; Accepted: December 3, 2010
Corresponding author: Yukihiro Hayatsu, MD. Department of Cardiovascular Surgery, Iwate Prefectural Central Hospital, 1-4-1 Ueda, Morioka, Iwate 020-0066, Japan
Tel: +81-19-653-1151, Fax: +81-19-653-2528
E-mail: haya_two@yahoo.co.jp



Fig. 1 Plain computed tomography of the patient. Acute aortic dissection was suspected from distal aortic arch to the level of diaphragm as the difference of CT values. Arrows mark dissecting portions.

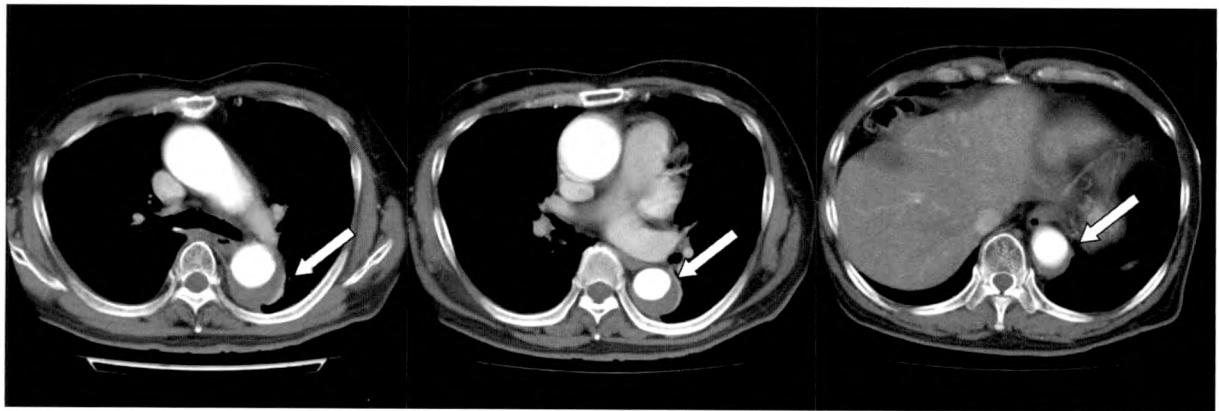


Fig. 2 Enhanced computed tomography of the patient. The computed tomography shows thrombosed aortic dissection from distal aortic arch to the level of the diaphragm. Arrows mark thrombosed dissecting portions.

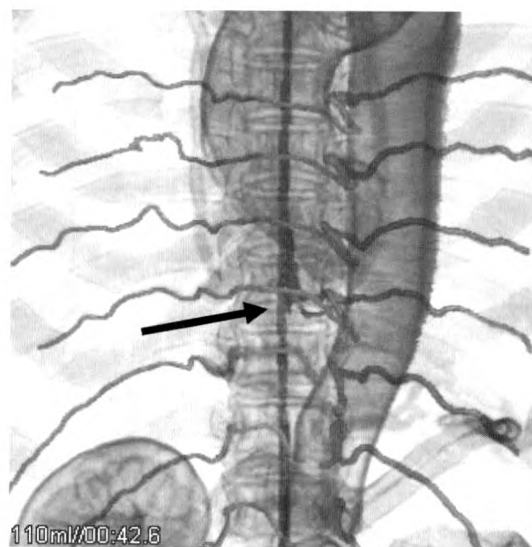


Fig. 3 Adamkiewicz artery arises from left 9th intercostal artery (arrow).

blood supply was pathognomonic in the perfusion area of anterior spinal artery. Especially, the anterior spinal artery below the level of Th4 is very narrow, and some of intercostal or lumbar arteries are very important sources of blood supply in this area. The largest and most important artery for an anterior spinal artery is called Adamkiewicz artery and it often arises from an intercostal artery between Th8 to L2. In this case, abrupt breakdown of blood flow to anterior spinal artery due to the thrombosed acute aortic dissection was the main cause of paraplegia. Furthermore, it was thought that collateral arteries such as the intercostal artery played a very important role to maintain Adamkiewicz artery flow, but it was not obvious in CT scan. And there are some mechanisms of spinal cord injury, the most important process is spinal cord edema after ischemia. Spinal cord edema increases CSF pressure and induces severe microcirculatory dysfunction which aggravates spinal cord circulation, moreover, and finally develops into paraplegia.^{3, 4)}

Effectiveness of CSF drainage for the prevention of paraplegia combined with thoracoabdominal aortic surgery is certified, and it is performed widely. However the therapeutic strategy for the paraplegia associated with acute aortic dissection is controversial. CSF drainage for the paraplegia with aortic dissection was first reported by Killen D et al. in 2000⁵⁾ and several reports have been presented since then. However, the effectiveness was not fully clarified, and it is unclear when CSF drainage should be started and when it should be discontinued. The longest case that had been reported from onset to SFD was 3.5 hours, though our case was 4 hours and the time from onset to CSF drainage may depend on the presence of collateral flow to anterior spinal cord. However, we thought that the usability of SFD up to 4 hours from onset was a remarkably safe and effective procedure for paraplegia from an acute aortic dissection.

On the other hand, the effectiveness of several drugs such as steroid, edaravone and naloxone⁶⁾ for paraplegia has been reported, but they are not fully effective. Our result demonstrated not only the effectiveness of CSF drainage for the paraplegia caused by acute aortic dissection, but also the time when it should be started and when discontinued.

Recently, Endovascular Aneurysm Repair (EVAR) has

been actively employed for thoracic aneurysm and the paraplegia is reported to occur at a frequency of 7%.⁷⁾ Although the risk of paraplegia associated with EVER is lower than that with surgical interventions, paraplegia is a serious complication and should be avoided. CSF drainage can also be a feasible and potential clinical option in that setting.

In conclusion, CSF drainage was remarkably effective for relief from paraplegia caused by acute aortic dissection. Paraplegia is a rare but devastating complication and so CSF drainage should be considered as the first choice in order to prevent paraplegia from progressing when the signs are observed in DeBakey acute aortic dissection.

REFERENCES

- 1) Zull DN, Cydulka R. Acute paraplegia: a presenting manifestation of aortic dissection. *Am J Med* 1998; **84**: 765–70.
- 2) Spittell PC, Spittell JA Jr, Joyce JW, Tajik AJ, Edwards WD, Schaff HV, et al. Clinical features and differential diagnosis of aortic dissection: experience with 236 cases (1980 through 1990). *Mayo Clin Proc* 1993; **68**: 642–51.
- 3) Safi HJ, Miller CC 3rd, Azizzadeh A, Iliopoulos DC. Observation on delayed neurological deficit after thoracoabdominal aortic aneurysm repair. *J Vasc Surg* 1997; **26**: 616–22.
- 4) Fleck T, Hutschala D, Weissl M, Wolner E, Grabenwöger M. Cerebrospinal fluid drainage as a useful treatment option to relieve paraplegia after stent-graft implantation for acute aortic dissection type B. *J Thorac Cardiovasc Surg* 2002; **123**: 1003–5.
- 5) Killen D, Weinstein C, Reed W. Reversal of spinal cord ischemia resulting from aortic dissection. *J Thorac Cardiovasc Surg* 2000; **119**: 1049–52.
- 6) Acher CW, Wynn MM, Hoch JR, Popic P, Archibald J, Turnipseed WD. Combined use of cerebral spinal fluid drainage and naloxone reduced the risk of paraplegia in thoracoabdominal aneurysm repair. *J Vasc Surg* 1994; **19**: 236–46.
- 7) Dake MD, Kato N, Mitchell RS, Semba CP, Razavi MK, Shimono T, et al. Endovascular stent-graft placement for the treatment of acute aortic dissection. *N Engl J Med* 1999; **340**: 1546–52.



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- 慢性動脈閉塞症に伴う潰瘍、疼痛及び冷感の改善
- 原発性肺高血圧症

<効能・効果に関連する使用上の注意> 原発性肺高血圧症

- (1) 原発性肺高血圧症と診断された患者にのみ使用すること。
- (2) 本剤は経口投与であるため、重症度の高い患者等では効果が得られにくい場合がある。循環動態あるいは臨床症状の改善が見られない場合は、注射剤や他の治療に切り替えるなど適切な処置を行うこと。

【用法・用量】

- 慢性動脈閉塞症に伴う潰瘍、疼痛及び冷感の改善 通常、成人には、ベラプロストナトリウムとして1日120 μ gを3回に分けて食後に経口投与する。
- 原発性肺高血圧症 通常、成人には、ベラプロストナトリウムとして1日60 μ gを3回に分けて食後に経口投与することから開始し、症状(副作用)を十分観察しながら漸次増量する。増量する場合には、投与回数を1日3~4回とし、最高用量を1日180 μ gとする。

<用法・用量に関連する使用上の注意> 原発性肺高血圧症

原発性肺高血圧症は薬物療法に対する忍容性が患者によって異なることが知られており、本剤の投与にあたっては、投与を少量より開始し、増量する場合は患者の状態を十分に観察しながら行うこと。

【使用上の注意】(抜粋)

1. 慎重投与(次の患者には慎重に投与すること) (1) 抗凝血剤、抗血小板剤、血栓溶解剤を投与中の患者(「相互作用」の項参照) (2) 月経期間中の患者[出血傾向を助長するおそれがある。] (3) 出血傾向並びにその素因のある患者[出血傾向を助長するおそれがある。]
2. 重要な基本的注意 (1) 本剤の有効成分は「ケアロードLA錠60 μ g」、「ベラスLA錠60 μ g」と同一であるが、原発性肺高血圧症において用法・用量が異なることに注意すること。(2) 原発性肺高血圧症において「ケアロードLA錠60 μ g」、「ベラスLA錠60 μ g」から本剤へ切り替える場合には、「ケアロードLA錠60 μ g」、「ベラスLA錠60 μ g」の最終投与時から12時間以上が経過した後に、本剤をベラプロストナトリウムとして原則1日60 μ gを3回に分けて食後に経口投与することから開始すること。また、「ケアロードLA錠60 μ g」、「ベラスLA錠60 μ g」と同用量の本剤に切り替えると、過量投与になるおそれがあるため注意すること。
3. 相互作用 併用注意(併用に注意すること) 抗凝血剤(ワルファリン等)、抗血小板小

板剤(アスピリン、チクロピジン等)、血栓溶解剤(ウロキナーゼ等)、プロスタグランジン₂製剤(エポプロステノール、ベラプロスト^{注1)})、エンドセリン受容体拮抗剤(ボセンタン)
注1) 同一有効成分を含有する「ケアロードLA錠60 μ g」、「ベラスLA錠60 μ g」等との併用に注意すること。

4. 副作用 ○慢性動脈閉塞症に伴う潰瘍、疼痛及び冷感の改善 総症例7,515例中、370例(4.9%)525件に副作用(臨床検査値異常を含む)が認められ、その主なものは頭痛91例(1.2%)、顔面潮紅60例(0.8%)、ほてり39例(0.5%)、下痢29例(0.4%)、嘔気20例(0.3%)等であった。(再審査結果通知:1999年3月)○**原発性肺高血圧症** 肺高血圧症の臨床試験において総症例40例中、24例(60.0%)65件に副作用(臨床検査値異常を含む)が認められ、その主なものは頭痛9例(22.5%)、LDH上昇5例(12.5%)、ビリルビン上昇4例(10.0%)、ほてり3例(7.5%)、下痢3例(7.5%)、嘔気3例(7.5%)、トリグリセリド上昇3例(7.5%)等であった。(効能追加時:1999年9月)
(1) **重大な副作用** 1) 出血傾向[脳出血(0.1%未満)、消化管出血(0.1%未満)、肺出血(頻度不明^{注2)})、眼底出血(0.1%未満)]; 観察を十分に行い、異常が認められた場合には投与を中止し、適切な処置を行うこと。2) ショック(0.1%未満): ショックを起こすことがあるので、観察を十分に行い、血圧低下、頻脈、顔面蒼白、嘔気等が認められた場合には投与を中止し、適切な処置を行うこと。3) 間質性肺炎(頻度不明^{注2)}): 間質性肺炎があらわれることがあるので、観察を十分に行い、異常が認められた場合には投与を中止し、適切な処置を行うこと。4) 肝機能障害(頻度不明^{注2)}): 黄疸や著しいAST(GOT)、ALT(GPT)の上昇を伴う肝機能障害があらわれることがあるので、観察を十分に行い、このような場合には投与を中止し、適切な処置を行うこと。5) 狭心症(頻度不明^{注2)}): 狭心症があらわれることがあるので、異常が認められた場合には投与を中止し、適切な処置を行うこと。6) 心筋梗塞(頻度不明^{注2)}): 心筋梗塞があらわれるとの報告があるので、異常が認められた場合には投与を中止し、適切な処置を行うこと。注2) 自発報告によるものについては頻度不明。

【承認条件】

原発性肺高血圧症において可能な限り、再審査期間中の全投与症例を使用成績調査の対象とすること。なお、予後に関する成績も収集すること。

■その他の使用上の注意等につきましては、製品添付文書をご参照ください。



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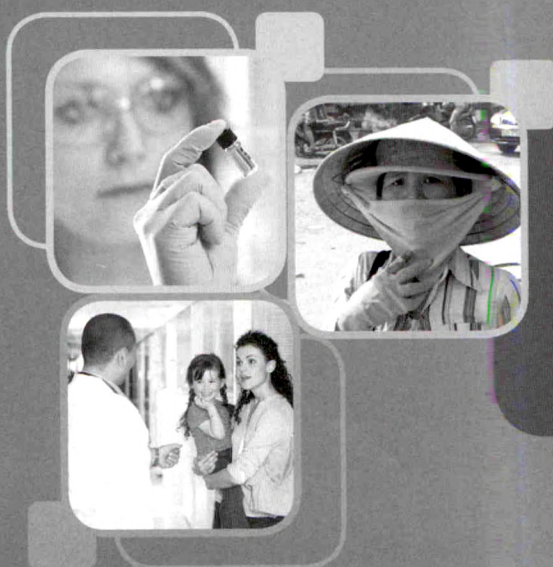


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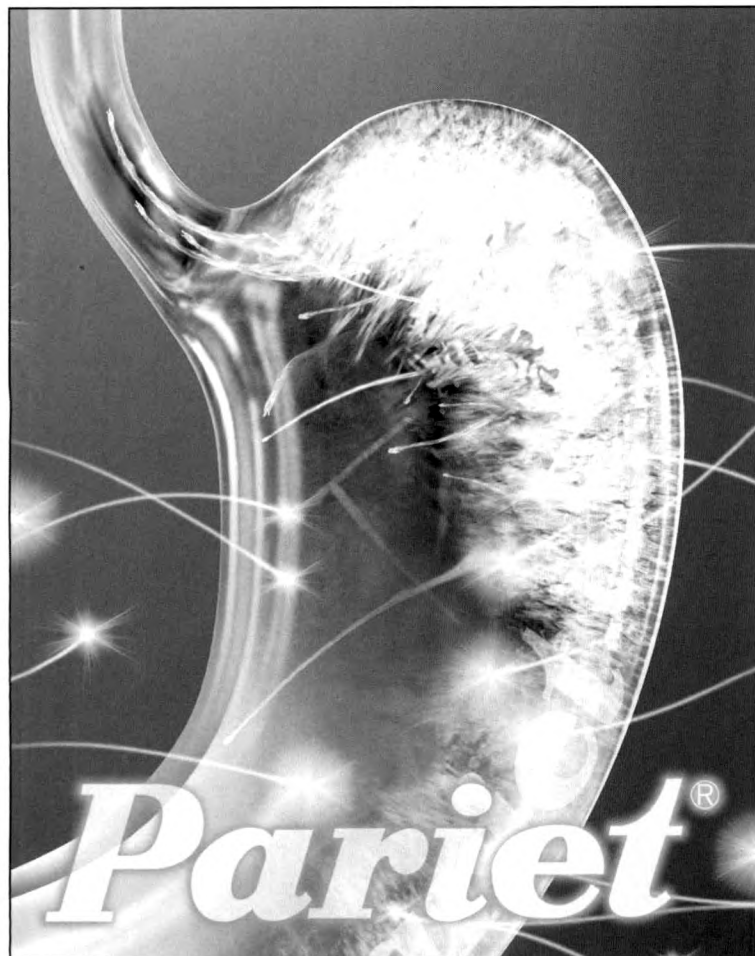
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► **Original Article** ◀

Correlation between Changes in Leg Blood Flow and Ankle-Brachial Pressure Index: A Study Using Laser Doppler Flowmeter —The 1st Report—

Kazuyoshi Suzuki, PT,^{1,2} Miho Sekiguchi, MD, PhD,² Hirofumi Midorikawa, MD, PhD,⁵ Koichi Sato, MD, PhD,⁴ Kazuyoshi Akase,⁵ Renshi Sawada, D.Eng,⁵ and Shin-ichi Konno, MD, PhD²

Objective: The objective of this study was to use non-invasive laser Doppler flowmeter to measure changes in blood flow in peripheral vessels in the legs before and after stress induced by leg elevation stress test and investigate correlations with the ankle-brachial pressure index (ABI).

Methods: Subjects included 28 patients over 20 years of age (mean, 73 years) who reported chiefly of leg symptoms such as intermittent claudication, numbness, chills, or cramps had been examined at the study institution, and agreed to participate in the study. The ABI of both legs was measured, and patients were divided into two groups: low ABI (ABI ≤ 0.9) and normal ABI (ABI ≥ 0.9). Blood flow in the big toe was measured using a box-type laser Doppler flowmeter before, during, and after leg-elevation stress. Amplitude of the recorded waveform and changes in blood flow were compared.

Results: Average ABI was 1.09 ± 0.10 in the normal ABI group (33 legs) and 0.68 ± 0.17 in the low ABI group (21 legs). Amplitude before and during stress was significantly smaller in the low ABI group than in the normal ABI group ($p < 0.01$), and there was a significant correlation with ABI before and during stresses ($r = 0.4606$, $r = 0.5048$, respectively; $p < 0.05$). Change in blood flow during stress was significantly lower in the low ABI group than in the normal ABI group ($p < 0.05$). There was a significant correlation between change in blood flow during stress and ABI in both groups ($r = 0.5073$; $p < 0.05$). There was also a significant correlation between change in blood flow and change in amplitude in both groups ($r = 0.5477$; $p < 0.05$).

Conclusion: Results of this study show, that comparing amplitude and change in blood flow before and after leg extension and elevation stress, there was a correlation between change in blood flow and amplitude, and ABI during stress. A box-type laser Doppler flowmeter may provide a means of screening for peripheral arterial disease.

Key words: peripheral arterial disease, ankle-brachial pressure index, laser Doppler flowmeter, intermittent claudication, lumbar spinal stenosis

¹Division of Rehabilitation, Iwase General Hospital, Sukagawa, Fukushima, Japan

²Department of Orthopedic Surgery, Fukushima Medical University School of Medicine, Fukushima, Fukushima, Japan

³Division of Cardiac and Vascular Surgery, Southern Tohoku Research Institute for Neuroscience, Southern Tohoku General Hospital, Koriyama, Fukushima, Japan

⁴Department of Cardiovascular Surgery, Sukagawa Hospital, Sukagawa, Fukushima, Japan

⁵Department of Intelligent Machinery and Systems, Graduate School of Engineering, Graduate School of Systems Life Sci-

ences, Microsystems and Bioengineering Lab, Kyushu University, Fukuoka, Fukuoka, Japan

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Corresponding author: Miho Sekiguchi MD, PhD. Department of Orthopedic Surgery, Fukushima Medical University School of Medicine, 1-Hikarigaoka, Fukushima, Fukushima 960-1295, Japan

Fax: +81-24-548-5505; Tel: +81-24-547-1276

E-mail: miho-s@fmu.ac.jp

INTRODUCTION

With the increasing aging of society, the incidence of arteriosclerosis-related disorders such as hypertension, and cardiovascular disease is rising. Peripheral arterial disease (PAD) and lumbar spinal stenosis (LSS) sometimes have similar symptoms and commonly occur around the same age; thus it is important to distinguish these underlying conditions.^{1,2)} The overall prevalence of PAD is 3%–10%, rising to 15%–20% over the age of 70 years.^{3–5)} The presence of arterial lesions in the legs reflects arterial lesions throughout the body, and the survival rate is poor.⁶⁾ It follows that PAD with intermittent vascular claudication requires early diagnosis and referral to a vascular specialist for early treatment. Measurement of the ankle-brachial pressure index (ABI) is an effective method of screening for PAD.^{7,8)} Pulse volume recording, toe brachial pressure index (TBI), Duplex ultrasonography, and magnetic resonance angiography are non-invasive methods for diagnosis of PAD.⁷⁾ ABI does not show blood flow of the leg tissue directly. Instead, ABI is determined using laser Doppler flowmeter (LDF) along with blood pressure measurements.^{9,10)} However, conventional LDF can only be used at rest and with patients maintaining the same position. If a simple, non-invasive method to measure blood flow in the leg were available that allowed for continual leg movement, it would enable screening for vascular lesions. A micro wireless flowmeter integrated laser Doppler blood flowmeter (MILDF) has been developed.^{11–13)} MILDF provides similar results to measurement of blood flow with conventional LDF. In addition, MILDF is wireless, portable, and allows monitoring of diurnal blood flow variation. The objective of this study was to use MILDF to measure changes in blood flow in the peripheral arteries of the leg before and after stress imposed by leg elevation stress test and to investigate their correlation with ABI.

SUBJECTS AND METHODS

Subjects were 28 patients over 20 years of age who had been examined at the study institution due to report chiefly related to leg symptoms such as intermittent claudication, numbness, chills, or cramps, and who provided informed consent to participate in the study. Subjects included 26 men and 2 women, with a mean age of 73 years (range, 57–91; most were in their 70s). This study was approved by the ethics committee of the facilities concerned.

ABI values were measured for both legs of the subjects. Subjects lay supine on a bed with blood pressure cuffs fitted to their upper arms and ankles on both sides, and their blood pressure was measured using a VaSera VS-1000 (Fukuda Denshi, Japan). Then, blood flow in both great toes was measured. The MILDF^{11–13)} used in this study was a box type that measured 5.6 mm × 12.0 mm × 17.5 mm and weighed 3 g (**Fig. 1**). This is approximately 1/300 the size of conventional LDF. Blood flow signals detected by the sensor were transmitted to the main unit, where measurement values were displayed. The main unit was also a signal transmitter, capable of sending data directly to a computer by Bluetooth operating on an industrial, science, and medical (ISM) 2.4–2.485 GHz wireless band. The blood flow waveform was continuously displayed on the computer screen and recorded from the data sent to the computer. As conventional LDF uses optical fibers for the input-output of laser light, movements of the optical fiber can result in noise. In this study, the fact that MILDF was wireless meant noise could be minimized. In addition, the miniaturized main unit also has the advantages of portability as well as the capability for continuous measurement and measurement during movement. It provides similar results to those of conventional LDF.^{11–13)} Measurements were performed in the outcome patient room at room temperature of 18°C. Only the subject and two observers were in the room during measurements.

The blood flow sensor was directly attached to the skin on one side of the great toe by double-sided tape. Subjects lay in the supine position, and blood flow measurements were started after subjects had spent at least 5 min resting on the bed. The blood flow waveform was checked on the computer screen, and blood flow was continuously recorded before, during, and after stress, as follows. Blood flow was measured for 60 seconds (s) in a resting state (before stress). Next, leg extension and elevation stress was imposed for 60 s, and blood flow was measured while the stress was imposed (during stress). The leg extension and elevation stress comprised elevating the leg in an extended position at an angle of 60° from the bed.¹⁴⁾ The leg was then returned to the bed, and blood flow was measured for 60 s after the stress had finished (after stress). Blood flow in the big toe of the opposite leg was also measured in the same way.

Blood flow waveform amplitude and change in blood flow were measured from the results obtained. Amplitude reflected each pulse beat. Amplitude was calculated from the waveform during each 60-s period before,

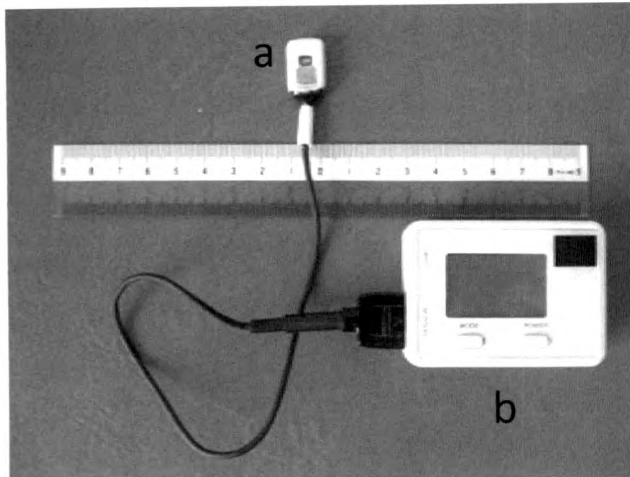


Fig. 1 Laser Doppler flowmeter.
(a) Box-type blood flow sensor and (b) portable flowmeter main unit.

during, and after stress by using 50-s periods excluding data from the 5 s before and after when the signal was affected by movement. Maximum and minimum amplitudes were selected from 10 points at 5-s intervals within the 50-s measurement periods, and the difference between them was taken as the amplitude size. Averages and standard deviations were calculated for the amplitudes at these 10 points before, during, and after stress, respectively. Change in amplitude was calculated by taking the amplitude before stress as 100% and calculating the change in average amplitude during and after stress, with amplitude before stress as the standard. Change in blood flow was calculated by using the waveform during 50-s intervals, excluding the 5 s before and after when the signal was affected by movement. The average of 2500 blood flow plots during these 50 s was calculated. Change in blood flow was calculated by taking blood flow before stress as 100% and calculating the averages and standard deviations of the changes in blood flow during and after stress.

Analysis was performed on two designated groups: one with normal ABI (ABI >0.9) and the other with low ABI (ABI ≤0.9).⁷⁾ Amplitude size and change in blood flow were compared between the two groups using a t-test. A *p* value less than 0.05 was considered significant. The significance level was set at a risk factor <5%. Pearson's product-moment correlation coefficient was used to investigate correlations between ABI, amplitude size, and change in blood flow. A *p* value of less than 0.05 was considered significant.

RESULTS

Analysis was performed on 54 of 56 legs in which blood flow was measured, excluding 2 legs for which the recorded waveform could not be analyzed. The normal ABI group comprised 33 legs, with an average ABI of 1.09 ± 0.10 . The low ABI group comprised 21 legs, with an average ABI of 0.68 ± 0.17 .

Blood flow waveform characteristics and amplitude size

Blood flow waveforms were characterized by a large amplitude in the normal ABI group and by a small amplitude in the low ABI group (**Fig. 2**). Amplitude before stress was 5.7 ± 2.8 ml (min 100 g) in the normal ABI group and 3.6 ± 2.5 ml (min 100 g) in the low ABI group. Amplitude was significantly smaller in the low ABI group than the normal ABI group ($p < 0.01$). There was a correlation between amplitude before stress and ABI ($r = 0.4606$; $p < 0.05$) (**Fig. 3a**).

Change in amplitude during stress

The change in amplitude during stress was $73.9\% \pm 62.2\%$ in the low ABI group and $108.7\% \pm 42.6\%$ in the normal ABI group. The amplitude was significantly decreased in the low ABI group compared with the normal ABI group ($p < 0.05$). The change in amplitude after stress was $100.9\% \pm 19.4\%$ in the low ABI group and $104.5\% \pm 23.8\%$ in the normal ABI group. There was no significant difference between the two groups. There was a correlation between change in amplitude during stress and ABI ($r = 0.5048$; $p < 0.05$) (**Fig. 3b**).

Change in blood flow during stress

The change in blood flow during stress was $44.5\% \pm 23.2\%$ in the low ABI group and $66.0 \pm 18.5\%$ in the normal ABI group. The blood flow was significantly decreased in the low ABI group compared with the normal ABI group ($p < 0.05$). The change in blood flow after stress was $116.2\% \pm 30.2\%$ in the low ABI group and $105.3\% \pm 22.3\%$ in the normal ABI group. There was no significant difference in change in blood flow between the two groups. There was a correlation between change in blood flow during stress and ABI ($r = 0.5073$; $p < 0.05$) (**Fig. 4**).

When the cut-off point of the blood flow change was defined as 60%, the flowmeter had a sensitivity of 71% and specificity of 58%. When cut-off point was 65%, the flowmeter had a sensitivity of 81% and a specificity of 55%.

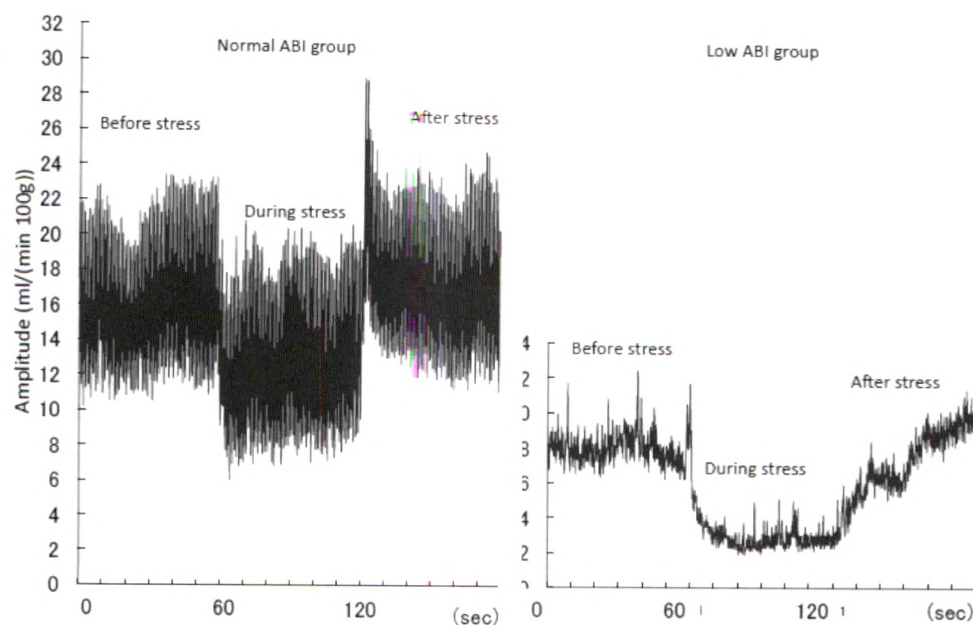


Fig. 2 Blood flow waveform characteristics.

The blood flow waveform in the normal ABI group was of large amplitude, whereas the amplitude was small in the low ABI group.

ABI, ankle-brachial pressure index

Change in amplitude and change in blood flow

There was a correlation between change in amplitude and change in blood flow ($r = 0.5477$; $p < 0.05$) (Fig. 5).

DISCUSSION

Measurement of ABI is a useful testing method for PAD diagnosis. ABI values ≤ 0.9 have 95% sensitivity for the arteriographic detection of PAD. Specificity for angiographically documented PAD is 90%.¹⁵⁾ ABI measurement is an essential requirement for PAD screening.^{16, 17)} Although devices are available for the simple calculation of ABI, the laser Doppler flowmeter used in this study has the advantages of being non-invasive and enabling continuous blood flow measurement. In our results, we found differences between the normal ABI and low ABI groups in the blood flow waveforms recorded. The amplitude of the waveform was significantly smaller in the low ABI group compared with the normal ABI group. The change in amplitude as a result of the imposition of leg extension and elevation stress was also smaller in the low ABI group. In addition, there was a positive correlation between change in amplitude size and ABI, meaning that it may be possible to carry out screening for PAD by measuring the change in

amplitude size before and during stress.

We found that the change in blood flow as a result of the imposition of leg extension and elevation stress was significantly lower in the low ABI group compared with the normal ABI group. This means that there is little variation in blood flow in patients with PAD despite the imposition of stress. When the cut-off point of blood flow change was 65%, MILDF had a sensitivity of 81% and specificity of 58% in this study. A decrease in blood flow of more than 65% during leg elevation stress compared with blood flow at the rest (before stress) might indicate PAD. MILDF might be useful in the screening of PAD; however, the results in the present study did not consider the severity of PAD. Furthermore, a study with a large sample size is needed to evaluate whether MILDF could show the severity of PAD. In addition, there was a correlation between amplitude and change in blood flow. These results suggest that blood vessels have weak reactivity in cases of suspected PAD. ABI reflects the stenosis or occlusion of large blood vessels in the legs, and there has been insufficient investigation to say whether or not it reflects blood flow in peripheral tissue. Nevertheless, the positive correlation between change in blood flow and ABI suggests the possibility that ABI can be predicted from change in blood flow before and after leg

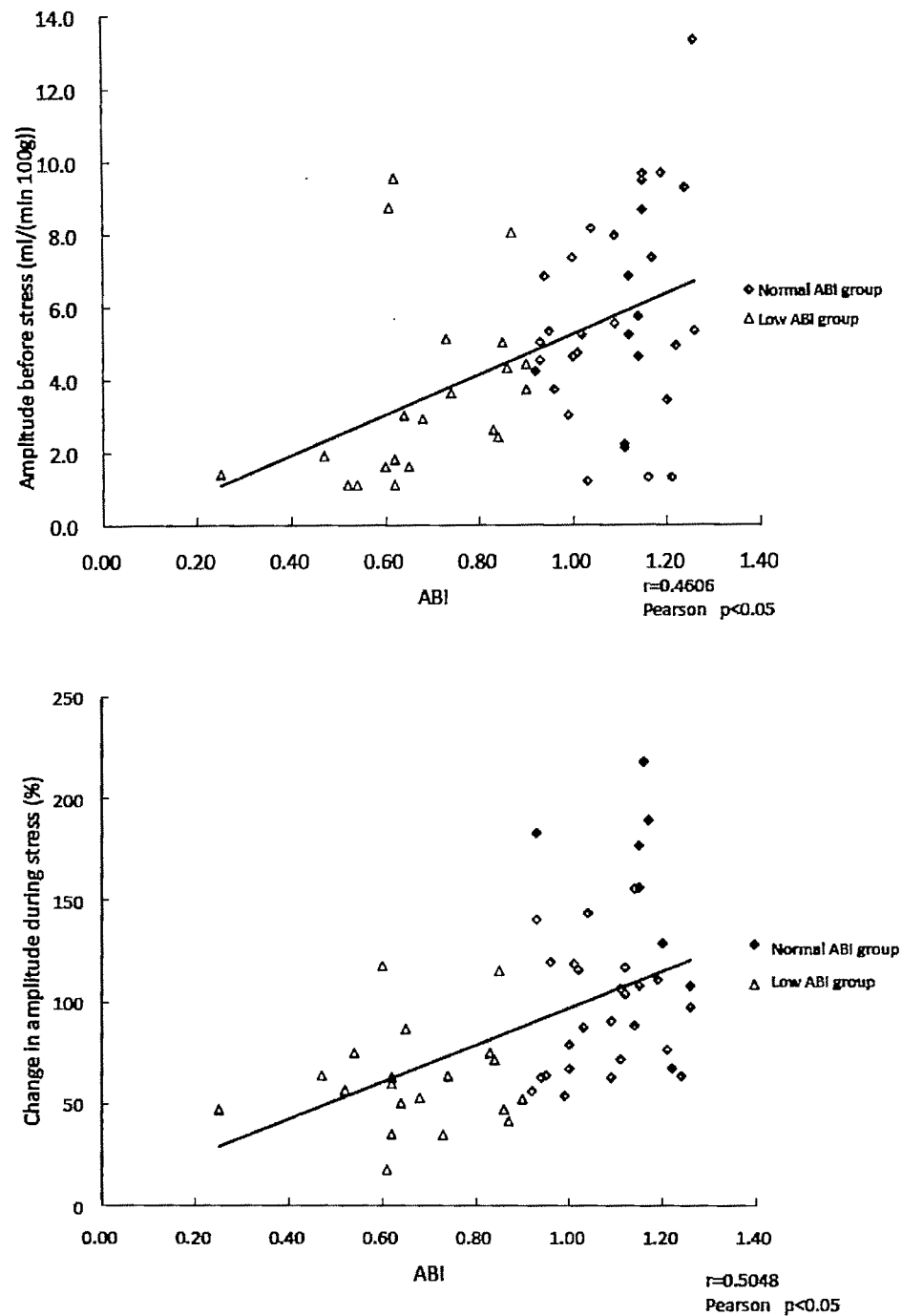


Fig. 3 Correlation between amplitude and ABI.

(a) Before stress

There was a correlation between amplitude and ABI before stress ($r = 0.4606$; $p < 0.05$).

(b) During stress

There was a correlation between change in amplitude (%) and ABI during stress ($r = 0.5048$; $p < 0.05$).

ABI, ankle-brachial pressure index

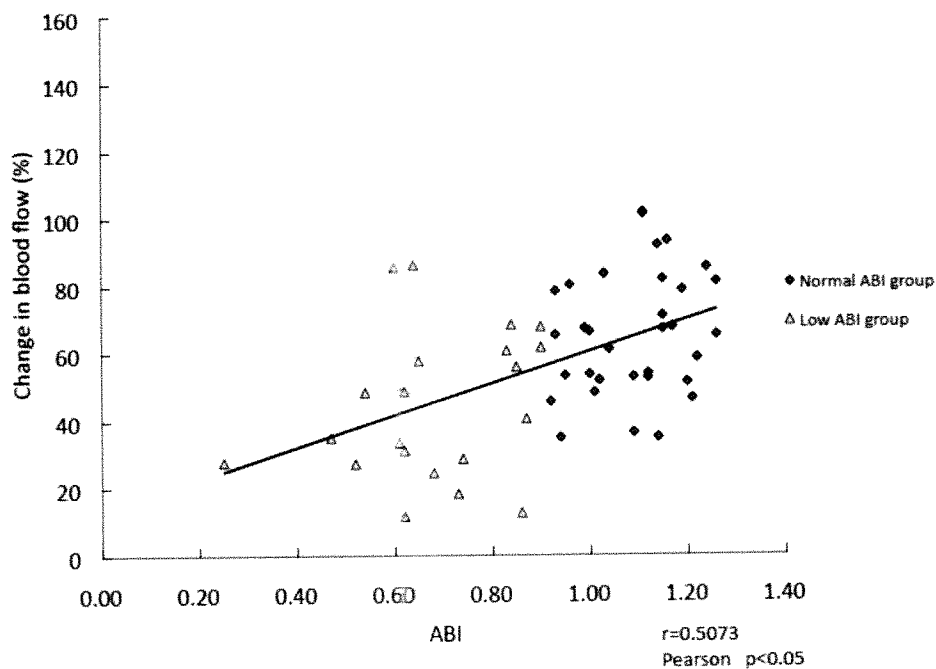


Fig. 4 Correlation between change in blood flow and ABI.
There was a correlation between change in blood flow and ABI ($r = 0.5073$; $p < 0.05$).
ABI, ankle-brachial pressure index

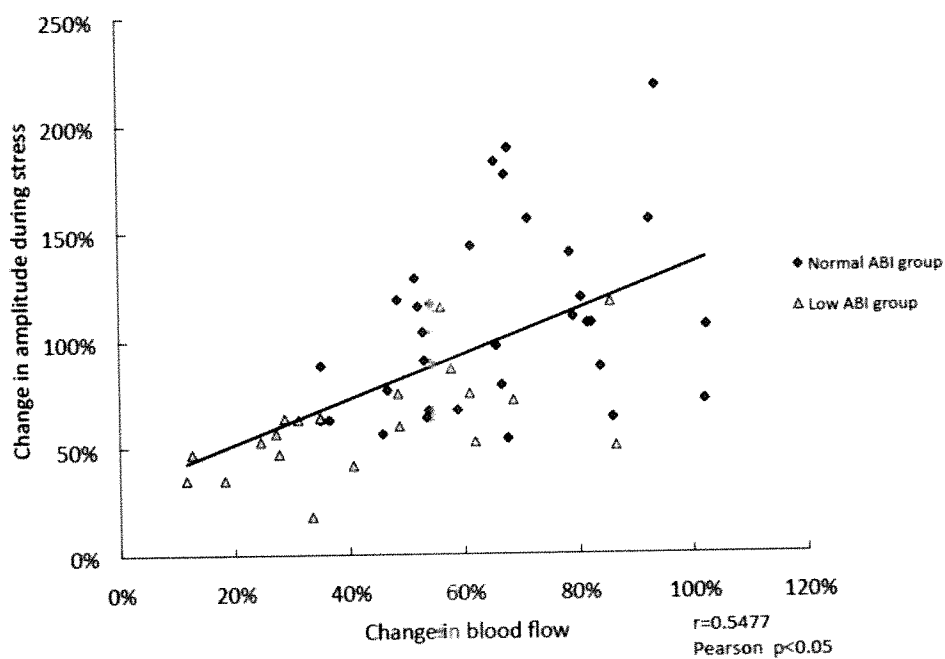


Fig. 5 Correlation between change in amplitude and change in blood flow.
There was a correlation between change in amplitude and change in blood flow ($r = 0.5477$; $p < 0.05$).

extension and elevation stress test. This study included only a small number of patients, however, and was limited by the fact that it was not possible to calculate the odds ratio for amplitude and change in blood flow that would constitute screening for PAD. If a large-scale study were carried out, this would enable the prediction of ABI from amplitude and change in blood flow. There are cases, however, in which it is not possible to obtain an accurate value for ABI because of a rise in ankle blood pressure due to diabetes, kidney failure, and vascular calcification. Cases which show false-positive ABI results should be examined using the TBI, which results in fewer false-positive findings compared with ABI. If TBI obtained by measuring blood pressure at the great toe is less than 0.7, then PAD is suspected.^{18, 19)} In a comparison of TBI and ABI among patients who underwent examination in a specialist vascular outpatient clinic, both ABI and TBI were low in 34% of cases.²⁰⁾ In 17% of cases, ABI was normal, and only TBI was low.²⁰⁾ Because the MILDF used in this study measured peripheral blood flow in the great toe, it may also be applicable to screening for vascular lesions in patients with other vascular disorders causing peripheral stenotic lesions, diabetes, and kidney failure. The present study, however, did not investigate whether there was any correlation among TBI, amplitude, and change in blood flow. Further research is required to determine whether there is any correlation between TBI and values measured by LDF. Further research is also required to determine whether PAD screening is possible in patients with PAD and LSS, both of which have characteristic symptoms of intermittent claudication and similar ages of onset. LSS is complicated by PAD in 6.7% of cases, occurs mainly in elderly people, and has a high frequency of cardiovascular complications.²¹⁾ Whether screening is possible in patients with LSS complicated by PAD requires further study.

The MILDF used in this study has also been reported as a useful testing device for evaluating therapeutic efficacy in skin disorders.²²⁾ It can also be anticipated to be of use as a tool for evaluating therapeutic efficacy in PAD patients. Further studies of blood flow waveform and changes in blood flow in PAD patients is required.

The MILDF used in this study can be used to screen for low ABI, by comparing amplitude and change in blood flow before and after leg extension and elevation stress. When the cut-off point of blood flow change using MILDF is 65%, sensitivity for PAD is 81%. Further study may enable LDF to be used as a simple PAD screening

tool in outpatient clinics other than specialist vascular departments.

REFERENCES

- 1) Verbiest H. A radicular syndrome from developmental narrowing of the lumbar vertebral canal. *J Bone Joint Surg Br* 1954; **36**: 230–7.
- 2) Verbiest H. Neurogenic intermittent claudication. Amsterdam: North-Holland, 1969: 79–150.
- 3) Criqui MH, Fronek A, Barrett-Connor E, Klauber MR, Gabriel S, Goodman D. The prevalence of peripheral arterial disease in a defined population. *Circulation* 1985; **71**: 510–5.
- 4) Hiatt WR, Hoag S, Hamman RF. Effect of diagnostic criteria on the prevalence of peripheral arterial disease. The San Luis Valley Diabetes Study. *Circulation* 1995; **91**: 1472–9.
- 5) Selvin E, Erlinger TP. Prevalence of and risk factors for peripheral arterial disease in the United States: results from the National Health and Nutrition Examination Survey, 1999–2000. *Circulation* 2004; **110**: 738–43.
- 6) Resnick HE, Lindsay RS, McDermott MM, Devereux RB, Jones KL, Fabsitz RR, et al. Relationship of high and low ankle brachial index to all-cause and cardiovascular disease mortality: the Strong Heart Study. *Circulation* 2004; **109**: 733–9.
- 7) Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG, et al. Inter-society consensus for the management of peripheral arterial disease (TASC II). *Eur J Vasc Endovasc Surg* 2007; **33**: S1–75.
- 8) Hirsch AT, Criqui MH, Treat-Jacobson D, Regensteiner JG, Creager MA, Olin JW, et al. Peripheral arterial disease detection, awareness, and treatment in primary care. *JAMA* 2006; **296**: 1335–44.
- 9) Dhindsa M, Sommerlad SM, DeVan AE, Barnes JN, Sugawara J, Ley O, et al. Interrelationship among noninvasive measures of postischemic macro- and microvascular reactivity. *J Appl Physiol* 2008; **105**: 427–32.
- 10) Mahe G, Leftheriotis G, Picquet J, Jaquinandi V, Sauzet JL, Abraham P. A normal penile pressure cannot rule out the presence of lesions on the arteries supplying the hypogastric circulation in patients with arterial claudication. *Vasc Med* 2009; **14**: 331–8.
- 11) Higurashi E, Sawada R, Ito T. An integrated laser blood flowmeter. *J Lightwave Technol* 2003; **21**: 591–5.
- 12) Kiyokura T, Mino S, Shimada J. Wearable micro laser blood flowmeter. *NTT Technical Journal* 2005; **11**: 24–7. (in Japanese).
- 13) Kiyokura T, Mino S, Shimada J. Wearable Blood Flowmeter. *NTT Technical Review* 2006; **4**: 38–43. (in Japanese).
- 14) Hoshino S, Kikuchi S, Watanabe T, Sato K, Seino H, Midorikawa H. Clinical guidebook for arteriosclerosis obliterans. Kita Media (Tokyo). 2002; 5–20. (in Japanese).

- nese)
- 15) Guo X, Li J, Pang W, Zhao M, Luo Y, Sun Y, et al. Sensitivity and specificity of ankle-brachial index for detecting angiographic stenosis of peripheral arteries. *Circ J* 2008; **72**: 605–10.
- 16) Ankle Brachial Index Collaboration, Fowkes FG, Murray GD, Butcher I, Heald CL, Lee RJ, et al. Ankle brachial index combined with Framingham Risk Score to predict cardiovascular events and mortality: a meta-analysis. *JAMA* 2008; **300**: 197–208.
- 17) Criqui MH, Ninomiya JK, Wingard DL, Ji M, Fronek A. Progression of peripheral arterial disease predicts cardiovascular disease morbidity and mortality. *J Am Coll Cardiol* 2008; **18**: 1736–42.
- 18) Bird CE, Criqui MH, Fronek A, Denenberg JO, Klauber MR, Langer RD. Quantitative and qualitative progression of peripheral arterial disease by non-invasive testing. *Vasc Med* 1999; **4**: 15–21.
- 19) Aboyans V, Criqui MH, Denenberg JO, Knoke JD, Ridker PM, Fronek A. Risk factors for progression of peripheral arterial disease in large and small vessels. *Circulation* 2006; **113**: 2623–9.
- 20) Matsui K, Ikeda U, Murakami Y, Yoshioka T, Suzuki T, Shimada K. Analysis of measurement of TBI for diagnosis of PAD. *J Jpn Coll Angiol* 2003; **43**: 536. (in Japanese)
- 21) Uesugi K, Sekiguchi M, Kikuchi S, Kanayama M, Takahashi K, Chiba K, et al. Lumbar spinal stenosis with peripheral disease. *ISSLS* 2010: GP141.
- 22) Kido M, Takeuchi S, Hayashida S, Urabe K, Sawada R, Furue M. Assessment of abnormal blood flow and efficacy of treatment in patients with systemic sclerosis using a newly developed microwireless laser Doppler flowmeter and arm-raising test. *Br J Dermatol* 2007; **157**: 690–7.

➤ Original Article ◀

Outcomes of Endovascular Intervention for Salvage of Failing Hemodialysis Access

Terence LX Tan, BMedSci, Kyin K May, MBBS, Peter A Robless, MD, MBChB, and Pei Ho, MBBS, FRCS, FHKAM

Objective: To investigate the effectiveness of endovascular balloon angioplasty to preserve the patency of failing hemodialysis arteriovenous fistulas (AVF) and prosthetic arteriovenous grafts (AVG).

Methods: Patients on hemodialysis who received endovascular intervention for access problems were retrospectively analyzed. Fistulography was performed on patients who were suspected to have access stenosis and balloon angioplasty performed in the same setting if a stenosis of $\geq 50\%$ is detected. Patients were followed up for post-operative complications and access restenosis or failure.

Results: 42 hemodialysis patients with 44 access sites (29 AVFs, 15 AVGs) required endovascular balloon angioplasty. There were no perioperative complications. Technical success rate was 100%. Median time from initial access creation to first balloon angioplasty was 13 months (2–146 months) for AVFs and 8 months (2–71 months) for AVGs. 19 of 44 patients subsequently developed restenosis. Median time for restenosis or access failure was 11 months (1–18 months) for AVFs and 5 months (1–10 months) for AVGs. Kaplan-Meier analysis for access patency after endovascular intervention showed 72% patency at 6 months and 32% at 12 months.

Conclusions: Endovascular balloon angioplasty is effective in restoring patency of failing hemodialysis accesses. Recurrence is common, and repeat interventions are required.

Key words: angioplasty, arteriovenous fistula, arteriovenous graft, renal failure, hemodialysis

INTRODUCTION

Autogenous arteriovenous fistulas (AVF) and prosthetic arteriovenous grafts (AVG) are necessary for chronic end-stage renal failure patients on hemodialysis. AVFs are the preferred initial hemodialysis access due to their longer patency than AVGs.¹ AVGs, however, remain

clinically important in patients whom AVFs are not feasible, and possibly in special populations such as the elderly.^{2–4}

Hemodialysis accesses are prone to failure due to thrombosis, usually concomitant with stenosis over the anastomosis or outflow vein. Access thrombosis frequently requires semi-emergent salvage intervention, but outcomes are generally unfavorable. Patients eventually may require multiple salvage procedures to restore functionality or creation of a new access. Some patients require placement of central venous catheters in the interim whilst the hemodialysis access becomes fully functional. Alternatively, to prevent access failure, clinicians can monitor the performance of these accesses and prophylactically provide interventions to rectify the hemodynamic problems and prolong their patency.⁵

Our service currently provides endovascular interventions to haemodialysis patients with failing access. This

Department of Cardiac, Thoracic and Vascular Surgery, National University Heart Centre, National University Hospital, Singapore

Received: November 7, 2010; Accepted: March 9, 2011
Corresponding author: Pei Ho, MBBS, FRCS, FHKAM. Department of Cardiac, Thoracic and Vascular Surgery, National University Heart Centre, National University Hospital, Singapore, 9/F NUHS Tower Block, 1E Kent Ridge Road, 119228, Singapore
Tel: +65-6772-2859, Fax: +65-6776-6475
E-mail: surhp@nus.edu.sg

Table 1 Patient demographics

	Total
Age (Mean $\pm$ SD)	59.8 $\pm$ 11.3
Sex: Male (%)	24 (57.1%)
Sex: Female (%)	18 (42.9%)
Diabetes mellitus	32 (73%)
Hypertension	37 (84%)
Ischaemic heart disease	18 (41%)
Hyperlipidaemia	25 (57%)
Peripheral vascular disease	9 (21%)
Stroke	6 (14%)
Smokers, active	6 (14%)

study aims to review the effectiveness of endovascular intervention for preservation of failing accesses.

PATIENTS AND METHODS

This study is approved by the institutional review board at our hospital. From August 2008 to March 2010, hemodialysis patients who received endovascular treatment for their dialysis access problem in the Vascular Surgery division of National University Hospital, Singapore, were retrospectively analyzed. The feature of failing AVFs or AVGs included one or more of the following: 1) Reduced thrill of vascular access assessed by clinical palpation by a vascular surgeon (P Ho), 2) Documented decreased dialysis flow rate defined by KDOQI guidelines⁶⁾ (access flow less than 600 ml/min, or less than 1000 ml/min with a more than 25% decrease over a four month period, 3) Documented increased venous pressure during dialysis as defined by KDOQI guidelines⁶⁾ (venous pressure of more than 150 mmHg or a trend of persistent increasing pressure over time) 4) Stenosis detected by duplex ultrasound, 5) Non-maturation of an AVF six weeks post-creation. Patient demographics and co-morbidities were documented.

Fistulograms were offered to all patients with one or more of the above-mentioned features of vascular access failure. The degree of stenosis in the peri-anastomotic region, fistula/graft, outflow vein and central veins were assessed during fistulography. Endovascular intervention in the form of balloon angioplasty was performed in the same setting if a stenosis of 50% or more of the vessel diameter is detected on angiography, using either a simple Wanda balloon (Boston Scientific, Natick, MA, USA) or a Peripheral cutting balloon (Boston Scientific, Natick, MA, USA). Cutting balloons were utilized for high grade

Table 2 Frequency of indication for fistulogram

Evidence of failing dialysis access	Number of cases (%)
Decreased dialysis flow rates	26 (59.1%)
Stenosis on duplex ultrasound	7 (15.9%)
Lack of fistula maturation	4 (9.1%)
Increased venous pressures	2 (4.5%)
Suspected thrombosis	2 (4.5%)
Difficulty in dialysis cannulation	2 (4.6%)
Poor thrill on clinical examination	1 (2.3%)

stenosis ($\geq 90\%$ stenosis) or total occlusion on fistulography, or when a simple balloon did not result in satisfactory restoration of access patency (re-stenosis $>50\%$). Completion fistulogram was performed immediately after angioplasty to determine success of the procedure. All patients were observed in the day surgery ward for two to three hours and discharged if no acute complications (bleeding or thrombosis) were detected. AVFs and AVGs, which were functional for dialysis pre-intervention, were used for dialysis the day after angioplasty.

Data are given as percentages and medians (range). Patency rates of hemodialysis access after initial salvage angioplasty were calculated according to the Kaplan-Meier method. Statistical analyses were performed using PASW Statistics 18 (IBM SPSS, Chicago, IL, USA). The fistulograms of the vascular accesses that require secondary intervention were reviewed to compare the sites of obstruction in the initial and subsequent intervention.

RESULTS

During the study period, 42 patients with a total of 44 hemodialysis accesses had stenosis confirmed by fistulogram and subsequently underwent balloon angioplasty for rectification of hemodynamic obstruction. 24 (57.1%) patients were male and 18 (42.9%) were female, with a mean age of 59.8 $\pm$ 11.3 (Range, 28–82). Medical co-morbidities were common among the studied population: 32 patients had diabetes mellitus (73%), 37 had hypertension (84%), 18 had ischaemic heart disease (41%), 25 had hyperlipidemia (57%), 9 had peripheral vascular disease (21%), and 6 had a history of stroke (14%). 6 of the patients were active smokers (14%) (**Table 1**).

Of the 44 hemodialysis accesses, 29 (65.9%) were AVFs, and 15 (34.1%) were AVGs. Frequencies of the

Table 3 Median time from access creation to first endovascular intervention

	Median (months)	Range (min-max)
AVF (n = 29)	13	2–146
AVG (n = 15)	8	2–71
Total (n = 44)	11	2–146

Table 4 Median time from first endovascular intervention to subsequent access failure

	Median (months)	Range (min-max)
AVF (n = 10)	11	1–18
AVG (n = 9)	5	1–10
Total (n = 19)	8	1–18

chief indication for fistulogram in the 44 accesses studied are listed in **Table 2**. As shown, the majority of patients were noted to have decreased access flow rates as measured during dialysis. The median time from access creation to the time of intervention was 13 months (Range, 2–146 months) for AVFs, and 8 months (Range, 2–71 months) for AVGs, yielding an average, median interval of 11 months (Range, 2–146) for all 44 accesses (**Table 3**).

The procedure success rate was 100%. No complications, notably bleeding and thrombosis, were detected after the interventions. Of the four non-mature AVFs, three eventually matured after angioplasty and was able to be used for dialysis. The remaining one AVF failed to mature, and this patient required the creation of a new vascular access. All other salvaged accesses were functional for dialysis immediately post-intervention.

After initial angioplasty, patients were followed up for a median of 5 months (Range, 1–18 months). 19 of the 44 (43.2%, 10 AVFs and 9 AVGs) accesses initially revised eventually failed again. There was no significant difference between the proportion of AVFs and AVGs that required a secondary procedure (34.5% AVFs, 60.0% AVGs, $p = 0.097$). On these 19 accesses, 11 accesses (57.9%) required a second angioplasty to restore patency, 5 (26.3%) thrombosed, and required the creation of new hemodialysis access, 1 (5.3%) required a jump graft, 1 (5.3%) required surgical revision, and 1 (5.3%) was converted to peritoneal dialysis after the access thrombosed.

Analysis of fistulographs of the 11 accesses that required a second angioplasty showed that stenosis recurred at the same site in 7 (63.6%) accesses, occurred in both the old and a new site in 2 (18.2%) accesses, extended contiguously in 1 (9.1%) access, and receded

from two sites to one in 1 (9.1%) access.

The median time from initial salvage angioplasty to re-intervention was 11 months (Range, 1–18 months) for AVFs and 5 months (Range, 1–10 months) for AVGs, yielding an average, median interval of 8 months (Range, 1–18 months) (**Table 4**). During the study period, four patients died from causes unrelated to hemodialysis access procedure (two from acute myocardial infarction, one from septic shock and one from a bleeding duodenal ulcer). Kaplan-Meier curves for hemodialysis accesses after initial balloon angioplasty showed a patency rate of 72% at 6 months and 32% at 12 months (**Fig. 1**).

DISCUSSION

Hemodialysis accesses in the form of AVFs or AVGs are integral to sustaining life in patients with established end-stage kidney disease. However, AVFs, and especially AVGs, are prone to stenosis and thrombosis which may preclude hemodialysis. Abandonment of a primary access frequently necessitates the creation of secondary and even tertiary accesses. The need for additional interventions⁷ in a group of patients already immunocompromised by renal disease results in increased hospital stays, increased economic costs,⁸ and increased morbidity and mortality.¹

Thus, it is important for nephrologists and vascular surgeons to adopt strategies that will minimize morbidity and maximize quality of life when dealing with patients on hemodialysis. In 2006, the Dialysis Outcomes Quality Initiative (DOQI) published by the US National Kidney Foundation¹ strongly recommended the placement of AVFs as a primary access for hemodialysis. This was based on research showing that patients with AVFs had a

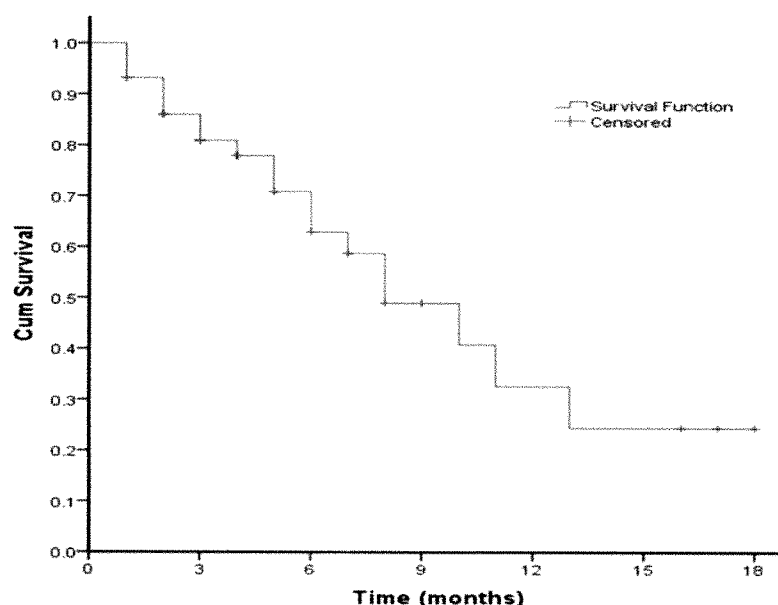


Fig. 1 Kaplan-Meier analysis for dialysis access patency after first endovascular intervention.

better overall quality of life than those with AVGs.⁹⁾ Indeed, most studies have subsequently showed that AVFs are beneficial compared to AVGs, with AVFs having greater primary patencies compared to AVGs.^{10–12)} This finding correlates with the results of the present study, where the median time needed from access creation to initial intervention was 13 months for AVFs, and 8 months for AVGs. Moreover, after the initial intervention, the time to develop restenosis or thrombosis was shorter in AVGs compared to AVFs. The shorter time taken for AVGs to develop stenosis and subsequent restenosis post-intervention indicates that patients with AVGs require more frequent interventions to maintain graft patency. AVGs, however, are nonetheless required in patients with inadequate upper arm veins and in those who have exhausted their autogenous venous capital. Some studies have shown that elderly³⁾ and diabetic patients²⁾ with AVGs have better access patency rates when compared to similar patients with AVFs, indicating that patient co-morbidities and demographics may play an important role in determining the best hemodialysis access type.

In this study, decreased flow rates and increased venous pressures measured during dialysis were the chief reasons suggesting that a patient's hemodialysis access was failing. This suggests that routine monitoring of access performance during dialysis is useful in picking up early access failure for salvage intervention. Some cli-

nicians advocate a regular surveillance program involving dialysis flow parameters^{1, 13)} or duplex ultrasound imaging,¹⁴⁾ in addition to standard of care clinical monitoring to detect and prophylactically intervene with failing hemodialysis accesses. Research has shown that regular surveillance may lead to improved quality of life for dialysis patients,¹⁵⁾ possibly from a reduction in the quantity of time spent in hospitals due to complications of access failure.¹⁶⁾ This benefit, however, has to be viewed in the context of unnecessarily exposing patients to increased numbers of salvage interventions as a consequence of routine surveillance.^{17, 18)} Importantly, there is substantial evidence that regular surveillance of AVGs may not decrease the risk of graft thrombosis,¹⁹⁾ nor prolong the time to graft abandonment.^{18, 20)} On the other hand, regular surveillance of AVFs does decrease the risk of access thrombosis,²¹⁾ but its effect on improving AVF patency is uncertain, with clinical trials producing conflicting results.^{21, 22)} Surveillance protocols using ultrasonography in previous studies have mostly monitored accesses every 3–4 monthly.^{18, 23, 24)} Given that the median time to initial and secondary intervention in this study for AVFs is 13 months and 11 months respectively, it is likely that a six-month surveillance programme will detect significant stenosis amenable to prophylactic intervention. A prospective comparative study investigating the patency rates of hemodynamic accesses and cost effectiveness under different surveillance intervals will

be needed to determine what the optimal surveillance interval should be. This longer interval between surveillance points may have the advantages of decreasing healthcare resources and costs required, also prevent patients from undergoing multiple unnecessarily procedures.

Percutaneous transluminal angioplasty (PTA) is the mainstay of treatment in stenosed hemodialysis access. With current techniques, PTA is a safe and useful intervention to restore access patency and preserve venous capital for future AVF or AVG creation.²⁵ PTA restores the luminal diameter of venous fistula by stretching and dissection of the vessel wall. This induces vascular damage and may cause subsequent restenosis.²⁶ Whether the mechanism of venous restenosis is similar to arterial restenosis is uncertain. However, in our experience, venous restenosis seems to recur more frequently than that of its arterial counterpart. Cutting balloon angioplasty reduces the amount of arterial wall damage by inducing a controlled fracture of atherosclerotic plaque. It is currently uncertain if cutting balloon angioplasty will reduce the recurrence rate of venous stenosis as compared to conventional balloon angioplasty. A recent study by Kariya et al.²⁷ showed no significant differences between these two techniques. Stenting of access stenosis is usually regarded as a second line option to balloon angioplasty and is usually performed only if balloon angioplasty is unsuccessful or with dissection. However, there is some evidence to suggest that stenting alone can improve patency outcomes in both AVFs and AVGs.²⁸ A recent study^{29, 30} has also shown that combined balloon angioplasty and stent-grafting confers an improved patency rate in AVGs with venous anastomotic stenosis over balloon angioplasty alone. It is not known if similar findings extend to AVFs.

CONCLUSION

Endovascular intervention in the form of balloon angioplasty is a safe and effective treatment for failing AVFs and AVGs. Re-stenosis is common and often requires further intervention in the form of repeat angioplasty.

REFERENCES

- 1) Gilmore J. KDOQI clinical practice guidelines and clinical practice recommendations-2006 updates. *Nephrol Nurs J* 2006; **33**: 487–8.
- 2) Woods JD, Turenne MN, Strawderman RL, Young EW, Hirth RA, Port FK, et al. Vascular access survival among incident haemodialysis patients in the United States. *Am J Kidney Dis* 1997; **30**: 50–7.
- 3) Chan MR, Sanchez RJ, Young HN, Yevzlin AS. Vascular access outcomes in the elderly haemodialysis population: A USRDS study. *Semin Dial* 2007; **20**: 606–10.
- 4) Richardson AI 2nd, Leake A, Schmieder GC, Biuckians A, Stokes GK, Panneton JM, et al. Should fistulas really be first in the elderly patient? *J Vasc Access* 2009; **10**: 199–202.
- 5) Turmel-Rodrigues L, Mouton A, Birmele B, Billaux L, Ammar N, Grézard O, et al. Salvage of immature forearm fistulas for haemodialysis by interventional radiology. *Nephrol Dial Transplant* 2001; **16**: 2365–71.
- 6) Foundation NK. KDOQI clinical practice guidelines and clinical practice recommendations for 2006 updates: haemodialysis adequacy, peritoneal dialysis adequacy and vascular access. *Am J Kidney Dis* 2006; **48** (suppl 1): S1–S322.
- 7) Hingorani A, Ascher E, Kallakuri S, Greenberg S, Khanimov Y. Impact of reintervention for failing upper-extremity arteriovenous autogenous access for haemodialysis. *J Vasc Surg* 2001; **34**: 1004–9.
- 8) Bittl JA, Cohen DJ, Seek MM, Feldman RL. Economic analysis of angiography and preemptive angioplasty to prevent haemodialysis-access thrombosis. *Catheter Cardiovasc Interv* 2009; **75**: 14–21.
- 9) Bazan HA. Why “fistula first” matters: increased durability, less interventions, and decreased costs. *Catheter Cardiovasc Interv* 2010; **75**: 22.
- 10) Hakim R, Himmelfarb J. Haemodialysis access failure: a call to action. *Kidney Int* 1998; **54**: 1029–40.
- 11) Coburn MC, Carney WI Jr. Comparison of basilic vein and polytetrafluoroethylene for brachial arteriovenous fistula. *J Vasc Surg* 1994; **20**: 896–902.
- 12) Matsuura JH, Rosenthal D, Clark M, Shuler FW, Kirby L, Shotwell M, et al. Transposed basilic vein versus polytetrafluoroethylene for brachial-axillary arteriovenous fistulas. *Am J Surg* 1998; **176**: 219–1.
- 13) Gallego Beuter JJ, Hernandez Lezana A, Herrero Calvo J, Moreno Carriles R. Early detection and treatment of haemodialysis access dysfunction. *Cardiovasc Intervent Radiol* 2000; **23**: 40–6.
- 14) Sands J, Young S, Miranda C. The effect of Doppler flow screening studies and elective revisions on dialysis access failure. *ASAIO J* 1992; **38**: M524–527.
- 15) Henry ML. Routine surveillance in vascular access for haemodialysis. *Eur J Vasc Endovasc Surg* 2006; **32**: 545–8.
- 16) Dossabhoy NR, Ram SJ, Nassar R, Work J, Eason JM, Paulson WD. Stenosis surveillance of haemodialysis grafts by duplex ultrasound reduces hospitalizations and cost of care. *Semin Dial* 2005; **18**: 550–7.
- 17) Wijnen E, Planken N, Keuter X, Kooman JP, Tordoir JH, de Haan MW, et al. Impact of a quality improvement programme based on vascular access flow moni-

- toring on costs, access occlusion and access failure. *Nephrol Dial Transplant* 2006; **21**: 3514–9.
- 18) Robbin ML, Oser RF, Lee JY, Heudebert GR, Menemeyer ST, Allon M. Randomized comparison of ultrasound surveillance and clinical monitoring on arteriovenous graft outcomes. *Kidney Int* 2006; **69**: 730–5.
- 19) Allon M, Robbin ML. Haemodialysis vascular access monitoring: current concepts. *Haemodial Int* 2009; **13**: 153–62.
- 20) Dember LM, Holmberg EF, Kaufman JS. Randomized controlled trial of prophylactic repair of haemodialysis arteriovenous graft stenosis. *Kidney Int* 2004; **66**: 390–8.
- 21) Tonelli M, James M, Wiebe N, Jindal K, Hemmelgarn B. Ultrasound monitoring to detect access stenosis in haemodialysis patients: a systematic review. *Am J Kidney Dis* 2008; **51**: 630–40.
- 22) Tessitore N, Lipari G, Poli A, Bedogna V, Baggio E, Loschiavo C, et al. Can blood flow surveillance and pre-emptive repair of subclinical stenosis prolong the useful life of arteriovenous fistulae? A randomized controlled study. *Nephrol Dial Transplant* 2004; **19**: 2325–33.
- 23) Scaffaro LA, Bettio JA, Cavazzola SA, Campos BT, Burmeister JE, Pereira RM, et al. Maintenance of haemodialysis arteriovenous fistulas by an interventional strategy: clinical and duplex ultrasonographic surveillance followed by transluminal angioplasty. *J Ultrasound Med* 2009; **28**: 1159–65.
- 24) Malik J, Tuka V, Chytilova E, Mokrejsova M, Masek M, Slavikova M. Low-flow polytetrafluoroethylene accesses: ultrasound surveillance and preemptive interventions ensure long-term patency. *Kidney Blood Press Res* 2010; **33**: 181–5.
- 25) Beathard GA. Fistula salvage by endovascular therapy. *Adv Chronic Kidney Dis* 2009; **16**: 339–51.
- 26) Davidson CJ, Newman GE, Sheikh KH, Kisslo K, Stack RS, Schwab SJ. Mechanisms of angioplasty in haemodialysis fistula stenoses evaluated by intravascular ultrasound. *Kidney Int* 1991; **40**: 91–5.
- 27) Kariya S, Tanigawa N, Kojima H, Komemushi A, Shomura Y, Shiraishi T, et al. Primary patency with cutting and conventional balloon angioplasty for different types of haemodialysis access stenosis. *Radiology* 2007; **243**: 578–87.
- 28) Chan MR, Bedi S, Sanchez RJ, Young HN, Becker YT, Kellerman PS, et al. Stent placement versus angioplasty improves patency of arteriovenous grafts and blood flow of arteriovenous fistulae. *Clin J Am Soc Nephrol* 2008; **3**: 699–705.
- 29) Dolmatch BL. Stent graft versus balloon angioplasty for failing dialysis access grafts: A long-awaited advance in the treatment of permanent haemodialysis access. *J Vasc Access* 2010; **11**: 89–91.
- 30) Haskal ZJ, Trerotola S, Dolmatch B, Schuman E, Altman S, Mietling S, et al. Stent graft versus balloon angioplasty for failing dialysis-access grafts. *N Engl J Med* 2010; **362**: 494–503.

► Original Article ◀

Improve Morbidity and Mortality in Coronary Artery Bypass Graft Surgery for Severe Atherosclerosis

Shinji Kanemitsu, MD, PhD,^{1,2} Sawaka Tanabe, MD,² Kensuke Ohue, MD,² Hiroyuki Miyagawa, MD,² Yoichiro Miyake, MD,² and Manabu Okabe, MD, PhD²

Objectives: Atherosclerosis has been identified as a risk factor for both morbidity and mortality in patients undergoing coronary artery bypass grafting (CABG). To investigate outcomes following CABG for severe atherosclerosis, and to determine whether different surgical techniques can reduce the risk of neurologic events in these patients.

Methods: We studied 225 consecutive patients who underwent elective isolated CABG. Routine preoperative and intraoperative examinations identified patients with severe atherosclerosis. We compared the outcomes between patients with (group A; 42 cases) and those without (group N; 183 cases) severe atherosclerosis.

Results: 36 patients (85.7%) in group A and 176 (96.2%) in group N underwent off-pump coronary artery bypass (OPCAB); 6 (14.3%) in group A and 7 (3.8%) in group N underwent on-pump beating CABG. Three patients in group A suffered deep sternal infection (7.1%), and one suffered stroke (2.4%) compared with none in group N. No cerebral infarction or neurologic events occurred in patients who underwent OPCAB (n = 212, 94.2%).

Conclusions: Prevalence of complications was significantly greater among patients with severe atherosclerotic disease who underwent OPCAB than in those without atherosclerotic disease. Careful selection of surgical strategies can prevent perioperative stroke and reduce mortality.

Key words: coronary artery bypass graft, off-pump coronary artery bypass, atherosclerosis, stroke, complications

INTRODUCTION

As society ages and the use of percutaneous coronary interventions increases, the preoperative condition of candidates for coronary artery bypass grafting (CABG) is becoming increasingly complex. The number

of patients with severe atherosclerosis has also recently increased. Severe atherosclerotic disease has been identified as an independent risk factor for mortality and stroke^{1,2)} in patients undergoing coronary revascularization, and can be associated with an operative mortality as high as 14.3%.³⁾ Careful choice of surgical techniques might reduce the risk of neurologic events in these patients. Off-pump coronary artery bypass (OPCAB) has gained worldwide popularity.^{4,5)} Comparative reports demonstrate significant reductions in mortality and major neurologic events following the use of OPCAB.^{6,7)} In this study, we compared the outcomes of CABG in patients with and without severe atherosclerosis. We investigated the hypothesis that different surgical techniques might prevent neurologic events and reduce mortality in those with severe atherosclerosis.

¹Department of Thoracic and Cardiovascular Surgery, Mie University Graduate School of Medicine, Tsu, Mie, Japan

²Division of Cardiovascular Surgery, Kochi Health Sciences Center, Kochi, Kochi, Japan

Received: September 6, 2010; Accepted: March 10, 2011
Corresponding author: Shinji Kanemitsu, MD, PhD. Department of Thoracic and Cardiovascular Surgery, Mie University School of Medicine, 2-174 Edobashi, Tsu, Mie 514-8507, Japan
Tel: +81-59-231-5021, Fax: +81-59-231-2845
E-mail: skanemitsu70@clin.medic.mie-u.ac.jp

PATIENTS AND METHODS

Patients

The final study population consisted of consecutive male and female patients who underwent elective isolated CABG at Kochi Health Sciences Center (Kochi, Japan) between January 2005 and September 2008. We compared the outcomes between patients with (group A) and those without (group N) severe atherosclerotic disease. As a retrospective study, this study did not require approval by our Institutional Review Board.

A total of 373 patients underwent CABG at our institution between January 2005 and September 2008. Elective isolated CABG was performed in 225 consecutive patients; they comprised the final study group. OPCAB was performed in 212 patients (94.2%). Preoperative and intraoperative screening identified 42 (18.7%) patients with severe atherosclerotic disease (group A). They were compared with those in group N (patients without atherosclerotic disease; n = 183, 81.3%).

Screening for atherosclerotic disease

We evaluated atherosclerotic lesions in all patients using routine, preoperative cervical vessel echography, thoracoabdominal computed tomography (CT), and intraoperative epiaortic echography. Patients were diagnosed with severe atherosclerotic disease (group A) if they met any of the following criteria:

- i. Carotid artery with severe stenosis (>70%) measured by the NASCET (North American Symptomatic Carotid Endarterectomy Trial) method.⁸⁾
- ii. Ascending aorta or aortic arch with an atherosclerotic lesion so severe that it was difficult and risky to maneuver it. Mild atheroma was defined as a localized atherosclerotic thickening of <3 mm, moderate atheroma as atherosclerotic thickening between 3–5 mm, and severe atheroma as atherosclerotic thickening >5 mm. Protruding or mobile plaques were recorded separately. We defined significant atheromatous disease (moderate-severe) as severe atherosclerotic disease.⁹⁾
- iii. Severe atherosclerotic lesion in the descending aorta, iliac arteries, or femoral arteries. In these cases, it was judged impossible to cannulate the extracorporeal circulation or perform intra-aortic balloon pumping (IABP) without undue risk.

Intraoperative examination of the ascending to the descending aorta was routinely performed by both transesophageal echocardiography (TEE) and epiaortic echography. When the patient had severe atherosclerosis

of the ascending aorta on TEE, echocardiography and manual palpation were performed to evaluate potential sites for arterial cannulation and side clamp application. In cases of an ascending aorta with a severe atherosclerotic lesion, we used a no-touch aorta technique and selected axillary cannulation if extracorporeal circulation was necessary. We used the method described by Wareing et al.⁹⁾ to classify and grade the severity of aortic atheromas.

Surgical procedures in coronary artery bypass grafting

The surgical methods did not change during the study. The majority of cases involved the use of our original OPCAB technique; this approach has been previously described; a series of techniques and instruments were developed to provide access to the circumflex area while hemodynamic stability was preserved, including the left pericardial traction technique, compression of the right pericardium, and a right sternal retractor.¹⁰⁾ We used cardiopulmonary bypass (CPB) in a standardized fashion, with a membrane oxygenator and a roller pump to perform OPCAB. We anastomosed proximal side under side aortic clamping, but we had no cross-clamping. No conventional CABG was performed in this study. All patients received 100 mg/day of aspirin before surgery; some also received clopidogrel (Plavix; Bristol-Myers Squibb/Sanofi Pharmaceuticals Partnership). All antiplatelet drugs were administered until surgery. Warfarin (Coumadin; Bristol-Myers Squibb, Princeton, New Jersey, USA) was titrated postoperatively to an international normalized ratio (INR) goal of 1.7–2.2. Many patients received continuous intravenous heparin (Hep-Lock, Liquaemin; Celsus Laboratories, Inc., Cincinnati, Ohio, USA) from the day after surgery until a target INR of 1.7 was achieved.

Diagnosis of brain infarction

Stroke was defined as the event of any new global or focal neurological deficit of presumed vascular origin lasting more than 24 h that could be evident soon after emergence from anesthesia (early stroke) or after first awakening without any neurological deficits (delayed stroke) until hospital discharge. A cerebrovascular accident diagnosed clinically either by an intensivist or neurologist was always confirmed by CT or magnetic resonance imaging. Stroke etiologies were identified and classified as either thromboembolism or hypoperfusion.

Table 1 Patient preoperative demographics

	Group N (n = 183)	Group A (n = 42)	p Value
Age	69.8 ± 8.9	75.3 ± 5.5	<i>p</i> <0.01
> 75 years old	68 (37.2%)	26 (61.9%)	<i>p</i> <0.001
Sex (male)	132 (72.1%)	35 (83.3%)	NS
Diabetes mellitus	72 (39.3%)	18 (42.8%)	NS
Hemodialysis	9 (4.9%)	4 (9.5%)	NS
Poor LVEF (<50%)	24 (13.1%)	6 (14.3%)	NS
Logistic EuroSCORE	3.16 ± 2.2	5.39 ± 2.9	<i>p</i> <0.001

LVEF, left ventricular ejection fraction

Table 2 Surgical characteristics

	Group N (n = 183)	Group A (n = 42)
Intra operative IABP	30 (16.4%)	2 (4.8%)
Conventional CABG	0 (0%)	0 (0%)
On-pump beating	7 (3.8%)	6 (14.3%)
Axillary artery cannulation	0 (0%)	4 (9.5%)
OPCAB	176 (96.2%)	36 (85.7%)
Aorta no-touch technique	74 (40.4%)	27 (64.3%)
Total distal anastomoses	3.0	2.6

IABP, intra aortic balloon pumping; CABG, coronary artery bypass grafting; OPCAB, off-pump coronary artery bypass

Statistical analysis

Patient data were collected retrospectively. Continuous variables are reported as means ± SD. Univariate analysis was carried out using the χ^2 test to determine significant differences. Fisher's exact test was used to analyze between-group differences in categorical variables. Statistical significance was set at *p* <0.05. We used SPSS version 11.0 (SPSS Inc, Chicago, IL, USA) to perform statistical analyses.

RESULTS

Preoperative demographics and cardiovascular risk factors are listed in **Table 1**. Group A had significantly more patients aged >75 years. Both groups were predominantly male, and almost 40% of patients had diabetes mellitus. In group A, four (9.5%) patients were receiving hemodialysis; this was not significantly different from group N. Poor left ventricular ejection function (<0.5) was present in six (14.3%) and 24 (13.1%) patients in groups A and N, respectively. The logistic EuroSCORE was significantly higher in group A than in group N (5.39 ± 2.9 vs. 3.16 ± 2.2, *p* <0.001).

Surgical characteristics are shown in **Table 2**. OPCAB was performed in 36 of 42 patients (85.7%) in group A, and 176 of 183 patients (96.2%) in group N; on-pump CABG was performed in 6 group A patients. The aorta no-touch technique was used more frequently in group A compared with group N [27 (64.3%) vs. 74 (40.4%); *p* <0.001]. In group A, axillary artery cannulation was performed in four of the six cases of CABG with on-pump beating. The mean numbers of distal anastomoses were 2.6 in group A and 3.0 in group N.

Postoperative complications and in-hospital mortality are shown in **Table 3**. All patients were in sinus rhythm on preoperative electrocardiogram. Postoperative atrial fibrillation occurred in six (14.3%) patients in group A compared with 23 (12.6%) in group N; the difference was not significant. Patients in group A were more likely to have other postoperative complications (including respiratory insufficiency and deep sternal infection). No one in group N suffered perioperative stroke. One patient in group A who underwent CABG with on-pump beating had a late stroke (watershed lesion infarction) 6 days after surgery. This was due to low perfusion. No cerebral infarction or neurologic defects occurred in OPCAB

Table 3 Complications and mortality

	Group N (n=183)	Group A (n=42)	p
Postoperative atrial fibrillation	23 (12.6%)	6 (14.3%)	NS
Prolonged respiratory failure	7 (3.8%)	3 (7.1%)	NS
Deep sternal infection	0 (0%)	3 (7.1%)	<0.001
Stroke	0 (0%)	1 (2.4%)	<0.05
In-hospital mortality	0 (0%)	0 (0%)	NS

patients (n = 212). No hospital death occurred in either group during the study period.

DISCUSSION

This study showed a significant association between severe atherosclerotic disease and increased incidence of postoperative complications, but not perioperative stroke. Our data suggest that severe atherosclerosis was associated with peripheral circulatory failure and deep sternal infections. Use of axillary artery cannulation, OPCAB, and the no-touch aorta technique reduced morbidity and mortality in those with severe atherosclerosis.

OPCAB has gained worldwide popularity^{4, 5)} and is associated with fewer postoperative complications and shorter lengths of stay in the hospital or intensive care unit than conventional CABG.⁴⁾ Nonrandomized studies report significant reductions in mortality and major neurologic events with OPCAB.^{6, 7)} In a comparison of OPCAB and conventional CABG, Mack et al.¹¹⁾ demonstrated that the elimination of CPB improved early survival in CABG patients, with a significant difference in mortality between the OPCAB and conventional CABG groups (1.9% vs. 3.5%). Other studies that compare OPCAB and conventional CABG also show that use of OPCAB in patients with severe atheromatous aortic disease is associated with significantly lower mortality, perioperative stroke, and overall complications.^{12, 13)} A recent case-matched report demonstrated a hospital survival benefit in specific high-risk OPCAB patients.¹³⁾ These findings are consistent with our outcomes.

Severe atherosclerosis of the ascending aorta and arch is known to increase the risk of mortality and perioperative stroke in CABG patients.¹⁾ In a recent review of more than 35000 patients, the stroke rate ranged from 0.9%–3.9% after isolated CABG, with a mean rate of 2%; stroke mortality ranged from 13%–25%.¹⁴⁾ Data show that the incidence of stroke remains high in patients with moderate or severe ascending aortic disease when CPB

(guided by epiaortic scanning) and minor modifications in surgical strategy are used,³⁾ and that mortality is excessive (24.8%) in patients who have a stroke.¹⁵⁾ Calafiore et al. note that limited or no manipulation of the ascending aorta in patients with severe atheromatous aortic disease is important.¹⁶⁾ We found that avoiding CPB and manipulation of the aorta improved outcomes in this subset of high-risk patients.

We routinely use intraoperative epiaortic scanning to identify atheromatous aortic disease in all patients scheduled to undergo CABG. If atheromatous aortic disease present, we use a no-touch technique for the aorta with OPCAB, or axillary artery cannulation and on-pump beating with CPB. These can be accomplished using *in situ* arterial grafts. In this study, identification of atherosclerosis of the ascending aorta by preoperative examination or intraoperative epiaortic scanning prompted the use of the aorta no-touch technique in 27 of 42 patients (64.3%). Wareing et al.³⁾ reported that when conventional CPB was used, the stroke rate was 1.1% in patients with normal or mild atherosclerosis, 3.0% in moderate cases, and 4.8% in those with severe atherosclerosis. These findings indicate that intraoperative screening of the ascending aorta might reduce the incidence of perioperative stroke.¹⁷⁾

It is not clear which options—avoiding CPB, avoiding aortic manipulation and proximal anastomosis, or eliminating CPB and aortic manipulation—might reduce the incidence of perioperative stroke. However, we had zero mortality using CPB, even in patients undergoing CABG under the on-pump beating. This suggests that CPB is not an independent risk factor for complications or mortality.

The proportion of strokes caused by aortic atheroemboli rather than concomitant cerebral atherosclerotic disease has not been clearly defined.¹⁸⁾ However, data show that use of varied surgical techniques can reduce the incidence of perioperative stroke. Depending on the location of the disease, varied surgical techniques have included a no-touch technique for the ascending aorta,

use of *in situ* arterial grafts, and modifications in sites of cannulation and proximal anastomoses. In this study, tailoring the surgical strategy to the results of cerebrovascular and aortic evaluations reduced morbidity from CABG-associated perioperative stroke.

Nakamura et al.¹⁹ found that intensive management of cerebral hemodynamics and atheromatous aorta reduced perioperative stroke in CABG patients. Prophylactic cerebrovascular interventions reduced stroke risk in those with poor cerebral perfusion reserve due to cerebrovascular atherosclerosis. We performed single photon emission computed tomography (SPECT) in a few patients in group A. One underwent superficial temporal artery to middle cerebral artery (STA-MCA) bypass, and another preoperative stent deployment in the carotid artery. No prior studies have shown any significant effect of STA-MCA bypass in preventing a subsequent stroke,²⁰ but the patient who underwent it prior to CABG did not suffer a stroke.

OPCAB techniques have recently been improved. Although cardiac output can be reduced during bypass of the left circumflex arteries, hypotension during anastomosis or conversion to CPB is rare. Nakamura et al.¹⁹ reported on the use of OPCAB without bypass of the diseased left circumflex arteries due to low aortic pressure. In this study, we safely performed off-pump coronary revascularization of the circumflex area using our original techniques and instruments, resulting in complete revascularization.

Moazami et al.²¹ reported that acute thrombosis may occur after cardiac surgery at the site of preexisting intracranial artery disease, but the administration of postoperative heparin did not independently reduce the risk of perioperative stroke. Perioperative management of aspirin therapy in patients undergoing coronary artery bypass surgery varies among surgeons and across medical institutions. Studies indicate that discontinuation of aspirin therapy before CABG is associated with reduced mortality, without significant increases in hemorrhage, blood product requirements, or related morbidities.^{22, 23} We continued preoperative antiplatelet therapy (aspirin, ticlopidine [Ticlid; Roche Laboratories, Nutley, New Jersey, USA] or clopidogrel), and administered postoperative heparin to all patients until their PT-INR was >1.7.

Increased thrombogenicity and fluctuating blood pressure due to postoperative low output syndrome or atrial fibrillation are potential mechanisms of late stroke.²⁴ Further studies of postoperative anticoagulation are needed to determine optimal strategies for preventing the

thrombotic occlusion of preexisting intracranial arterial stenosis.

Limitations

The limitations of this study include its small sample size, the use of retrospective patient data, the absence of a control group, and the fact that no patients underwent CABG using conventional on-pump techniques. Intensive management of cerebral vascular disease may have been useful, but was not performed because of increased cost. The strength of this study was the lack of a learning curve for OPCAB surgery; only a few experienced surgeons have been performing by the unified techniques since 1999.

CONCLUSIONS

Although there was no mortality among patients undergoing elective isolated CABG, postoperative morbidity (deep sternal infection and stroke) was higher in those with severe atherosclerotic disease than in those without it. Data suggest that we can prevent perioperative stroke and minimize neurologic complications by tailoring surgical strategies (e.g., use of OPCAB, the aorta no-touch technique, or axillary artery cannulation) in patients with severe atherosclerosis.

Preoperative vascular evaluation and tailored surgical strategies (various surgical techniques and perioperative drug management; antiplatelet and anticoagulation therapy) are critical to prevent complications, such as cerebral infarction, and to improve outcomes after CABG. Nonetheless, other complications in patients with severe atherosclerosis remain a problem. Therefore, we suggested that perioperative blood glucose control and respiratory management become the most important to prevent other complications in patients with very severe atherosclerosis. Further studies are required to determine the costs and benefits of a more aggressive approach to preoperative vascular evaluation in patients requiring CABG.

REFERENCES

- 1) Roach GW, Kanchuger M, Mangano CM, Newman M, Nussmeier N, Wolman R, et al. Adverse cerebral outcomes after coronary bypass surgery. Multicenter Study of Perioperative Ischemia Research Group and the Ischemia Research and Education Foundation Investigators. *N Engl J Med* 1996; **335**: 1857–63.
- 2) Davila-Roman VG, Murphy SF, Nickerson NJ, Kou-

- choukos NT, Schechtman KB, Barzilai B. Atherosclerosis of the ascending aorta is an independent predictor of long-term neurologic events and mortality. *J Am Coll Cardiol* 1999; **33**: 1308–6.
- 3) Wareing TH, Davila-Roman VG, Daily BB, Murphy SF, Schechtman KB, Barzilai B, et al. Strategy for the reduction of stroke incidence in cardiac surgical patients. *Ann Thorac Surg* 1993; **55**: 1400–8.
- 4) Hart JC, Puskas JD, Sabik JF 3rd. Off-pump coronary revascularization: current state of the art. *Semin Thorac Cardiovasc Surg* 2002; **14**: 70–81.
- 5) Meharwal ZS, Mishra YK, Kohli V, Bapna R, Singh S, Trehan N. Off-pump multivessel coronary artery surgery in high-risk patients. *Ann Thorac Surg* 2002; **74**: S1353–7.
- 6) Al-Ruzzeh S, George S, Yacoub M, Amrani M. The clinical outcome of off-pump coronary artery bypass surgery in the elderly patients. *Eur J Cardiothorac Surg* 2001; **20**: 1152–6.
- 7) Al-Ruzzeh S, Nakamura K, Athanasiou T, Modine T, George S, Yacoub M, et al. Does off-pump coronary artery bypass (OPCAB) surgery improve the outcome in high-risk patients? A comparative study of 1398 high-risk patients. *Eur J Cardiothorac Surg* 2003; **23**: 50–5.
- 8) Moneta GL, Edwards JM, Chitwood RW, Taylor LM Jr, Lee RW, Cummings CA, et al. Correlation of North American Symptomatic Carotid Endarterectomy Trial (NASCET) angiographic definition of 70% to 99% internal carotid artery stenosis with duplex scanning. *J Vasc Surg* 1993; **17**: 152–9.
- 9) Wareing TH, Davila-Roman VG, Barzilai B, Murphy SF, Kouchoukos NT. Management of the severely atherosclerotic ascending aorta during cardiac operations: A strategy for detection and treatment. *J Thorac Cardiovasc Surg* 1992; **103**: 453–62.
- 10) Suzuki T, Okabe M, Yasuda F, Miyake Y, Handa M, Nakamura T. Our experiences for off-pump coronary artery bypass grafting to the circumflex system. *Ann Thorac Surg* 2003; **76**: 2013–6.
- 11) Mack M, Bachand D, Acuff T, Edgerton J, Prince S, Dewey T, et al. Improved outcomes in coronary artery bypass grafting with beating-heart techniques. *J Thorac Cardiovasc Surg* 2002; **124**: 598–607.
- 12) Mishra M, Malhotra R, Karlekar A, Mishra Y, Trehan N. Propensity case-matched analysis of off-pump versus on-pump coronary artery bypass grafting in patients with atheromatous aorta. *Ann Thorac Surg* 2006; **82**: 608–14.
- 13) Sharony R, Grossi EA, Saunders PC, Galloway AC, Applebaum R, Ribakove GH, et al. Propensity case-matched analysis of off-pump coronary artery bypass grafting in patients with atheromatous aortic disease. *J Thorac Cardiovasc Surg* 2004; **127**: 406–13.
- 14) Engelman DT, Cohn LH, Rizzo RJ. Incidence of predictors of TIAs and strokes following coronary artery bypass grafting report and collective review. *Heart Surg Forum* 1999; **2**: 242–5.
- 15) John R, Choudhri AF, Weinberg AD, Ting W, Rose EA, Smith CR, et al. Multicenter review of preoperative risk factors for stroke after coronary artery bypass grafting. *Ann Thorac Surg* 2000; **69**: 30–6.
- 16) Calafiore AM, Di Mauro M, Teodori G, Di Giammarco G, Cirmeni S, Contini M, et al. Impact of aortic manipulation on incidence of cerebrovascular accidents after surgical myocardial revascularization. *Ann Thorac Surg* 2002; **73**: 1387–93.
- 17) Hangler HB, Nagele G, Danzmayr M, Mueller L, Ruttman E, Laufer G, et al. Modification of surgical technique for ascending aortic atherosclerosis: impact on stroke reduction in coronary artery bypass grafting. *J Thorac Cardiovasc Surg* 2003; **126**: 391–400.
- 18) Trehan N, Mishra M, Kasliwal RR, Mishra A. Reduced neurological injury during CABG in patients with mobile aortic atheromas a five-year follow-up study. *Ann Thorac Surg* 2000; **70**: 1558–64.
- 19) Nakamura M, Okamoto F, Nakanishi K, Maruyama R, Yamada A, Ushikoshi S, et al. Does intensive management of cerebral hemodynamics and atheromatous aorta reduce stroke after coronary artery surgery? *Ann Thoracic Surg* 2008; **85**: 513–9.
- 20) The EC/IC Bypass Study Group. The International Cooperative Study of Extracranial/Intracranial Arterial Anastomosis (EC/IC Bypass Study): methodology and entry characteristics. *Stroke* 1985; **16**: 397–406.
- 21) Moazami N, Smedira NG, McCarthy PM, Katzan I, Sila CA, Lytle BW, et al. Safety and efficacy of intraarterial thrombolysis for perioperative stroke after cardiac operation. *Ann Thorac Surg* 2001; **72**: 1933–9.
- 22) Bybee KA, Powell BD, Valeti U, Rosales AG, Kopecky SL, Mullany C, et al. Preoperative aspirin therapy is associated with improved postoperative outcomes in patients undergoing coronary artery bypass grafting. *Circulation* 2005; **112**: 1286–92.
- 23) Mangano DT. Multicenter Study of Perioperative Ischemia Research Group: Aspirin and mortality from coronary bypass surgery. *N Engl J Med* 2002; **347**: 1309–7.
- 24) Stamou SC, Hill PC, Dangas G, Pfister AJ, Boyce SW, Dullum MK, et al. Stroke after coronary artery bypass: incidence, predictors, and clinical outcome. *Stroke* 2001; **32**: 1508–3.

► Original Article ◀

Platelet Nitric Oxide Signaling System in Patients with Coronary Artery Disease

Mahdi Garelnabi, PhD,¹ Vinod Gupta, MD,² Venkatesan Mallika, MD,² and Jayashree Bhattacharjee, MD³

Background: Coronary artery disease (CAD) is the leading cause of death worldwide, and the major cause of hospital admissions in the Western countries. The pathogenesis of CAD is closely related to nitric oxide release and formation. The purpose of this study was to investigate the status of platelets nitric oxide in patients with coronary artery disease.

Methods: We measured platelets aggregation, cGMP, NO (nitrite/nitrate level), NO synthase activity, plasma NO, and ionized Ca²⁺ in 40 healthy volunteers and 120 patients with myocardial infarction, unstable and stable angina, with 40 subjects in each group. The subjects' age mean range was from 40–51 years.

Results: Platelets aggregation, NO, cGMP, NO synthase activity, plasma NO and ionized Ca²⁺ have increased significantly ($P < 0.001$) across the patients groups compared to controls. Platelets NO synthase activity (mean $\pm$ SD / U / 10⁹ platelets) in healthy controls, MI, unstable angina and stable angina patients were 1.19 ± 0.56 , 1.21 ± 0.64 , 1.64 ± 0.98 and 1.57 ± 0.81 respectively. The cGMP (mean $\pm$ SD / pmole / 10⁹ platelets) levels were 0.95 ± 0.41 , 1.53 ± 0.64 , 3.18 ± 0.77 , and 5.12 ± 1.5 respectively.

Conclusions: The present study demonstrated that platelets aggregation, NO, cGMP, NO synthase activity, plasma NO, and ionized Ca²⁺ profoundly increased in CAD. The increases in NO-cGMP components may have resulted as a compensatory response to ameliorate platelet activity and Ca²⁺ levels in CAD patients.

Key words: cardiovascular disease, heart disease, nitric oxide, platelets, ischemic heart disease

INTRODUCTION

Coronary artery disease (CAD) is the leading cause of death worldwide and the major cause of hospital admissions in Western countries.¹⁾ The disease is a manifest of a progressive atherosclerosis disease that develops

from early childhood through a complex process mediated by inflammation and oxidative stress.^{2–4)} Platelet contributes to the pathogenesis of cardiovascular disease, and its involvement in the pathogenesis of thrombosis-related complications is well-documented.²⁾

The nitric Oxide-Cyclic GMP signal transduction system has emerged as a ubiquitous pathway for intracellular and intercellular communication.⁵⁾ Although NO release is known to improve endothelium performance and inhibit platelets function, NO may also forms the potent peroxynitrite that in turn, contributes to the oxidative damage. Nitric oxide derived reactive nitrogen species (RNS), such as nitrogen dioxide (NO₂) and peroxynitrite (ONOO⁻), are believed to mediate cellular oxidative damage. When NO is in excess of that required to activate guanylate cyclase, it can inhibit glycolysis, the mitochondria c respiratory chain and DNA replication.^{6, 7)} The pathogenesis of CAD is closely related to nitric oxide release and formation. Several studies suggest that the

¹Department of Clinical Laboratory and Nutritional Sciences, University of Massachusetts Lowell, Massachusetts, USA

²Department of Clinical Biochemistry, G. B. Hospital and MA Medical College, New Delhi, India

³Department of Biochemistry, Lady Hardings Medical College, New Delhi, India

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Corresponding author: Mahdi Garelnabi, PhD. Department of Clinical Laboratory and Nutritional Sciences, School of Health and Environment, University of Massachusetts Lowell, 61 Wilder, Lowell, Suite 319, Lowell, Massachusetts 01854, USA
Tel: +1-978-934-4528, Fax: +1-978-934-4021
E-mail: Mahdi_Garelnabi@uml.edu

basal release of NO by the endothelium contributes to the regulation of vascular tone,⁸⁾ blood flow, and blood pressure. NO inhibits platelet aggregation and adhesion to vascular endothelium. In addition, NO inhibits leukocyte adhesion to endothelium.⁹⁾ Alteration of cellular calcium homeostasis is also a critical event in ischemic heart injury. NO, released by the endothelium or synthesized by platelets, participates in the regulation of Ca^{2+} signaling. The elevation of cGMP, as a result of the activation of guanylate cyclase by NO, stimulates a number of mechanisms that actively decrease calcium levels within the cell.¹⁰⁻¹⁴⁾ Although the NO-cGMP signaling system is immensely investigated; sparse data are available pertaining to the role of platelet NO activity in CAD. The current study was designed to investigate the NO-cGMP system in patients with CAD.

MATERIALS AND METHODS

All chemicals and reagents were of analytical grade. Naphthylenediamine, sulfanilamide, HEPES, ADP, nitrate reductase, methemoglobin and dithiothreitol were purchased from Sigma Chemical Co. USA; Radiometer, Denmark; reagents used for the determination of ionized Calcium (Ca^{2+}). cGMP ELISA kit was purchased from Biomedical Technologies Inc., USA. The remainder of chemicals were purchased from Merck, Germany.

Study design

Recruitment and analysis were completed at G. B Pant Hospital and Mulana Azad Medical College, New Delhi, India.

Study population: All subjects completed and signed a consent form explaining the voluntary nature of the study. The research protocol was approved by MA Medical College and G B Pant Hospital Institutional Review Board. The patients' population consisted of 120 subjects diagnosed with ischemic heart diseases during their visit to the New Delhi city metropolitan Emergency Unit of LNJP Hospital and the Department of Cardiology at G.B. Pant Hospital. The patients initially complained of chest pain and were later diagnosed with ischemic heart diseases, according to the criteria of the New York Heart Association.¹⁵⁾ Patients with primary coagulopathy, bleeding diathesis, diabetes, or any other disease known to alter platelet activity, were excluded from the study. In addition, those who underwent angiographic imaging studies and their findings failed to match with the criteria for the disease, or on drugs that may affect platelet

function or on prescribed lipid-lowering drugs, were dropped from the study. A group of 40 apparently healthy individuals, who belongs to similar socio-economic demography as that of the patients, and without any history suggestive of coronary artery disease were selected for the study from volunteers visiting the Blood Bank and the Out Patients Department (OPD) of G.B. Pant Hospital.

Blood samples: 20 mL blood from fasting subjects was collected in vials containing 3.8% trisodium citrate anticoagulant and mixed gently by inversion. The platelet count was performed immediately as previously described.¹⁶⁾ Blood samples in plain vials were also collected and centrifuged at 2500 rpm, and serum was obtained. Platelet Rich Plasma (PRP) was prepared by centrifugation of the citrated blood at 1000 rpm for 15 minutes at 37°C using polyethylene test tubes. The process for the PRP and platelets pellets preparation was completed within the first hour of the blood collection according to Fraser et al.¹⁷⁾

Biochemical assays: Using enzymatic methods, serum total cholesterol (TC), triglycerides (TG), and high-density lipoproteins (HDL) were determined by reagents purchased from E. Merck (India), using an Olympus AU400 chemistry analyzer.

Determination of platelets aggregation: Platelet aggregation was determined in the PRP by a previously described method¹⁷⁾ using Chrono Log aggregometer model 560-CA make of Chrono Log Corporation of USA.

Measurement of ionized calcium (Ca^{2+}): Ionized Calcium Ca^{2+} in plasma was determined using ICA2 ionized calcium analyzer, of Radiometer, Copenhagen, Denmark.

Measurement of nitric oxide: Nitric Oxide (NO) as nitrite/nitrate level in plasma or washed platelets suspensions determined indirectly, by the measurement of the stable by-products nitrate and nitrite, employing the Griess's reaction according to the method of Mathew et al.¹⁸⁾ Briefly, in an oxygenated solution NO decomposes to form NO_2^- and NO_3^- . These stable products can be determined using a spectrophotometer assay. Nitrite is measurable by observing the magenta-colored azo dye that is formed from NO_2^- and the Griess's reagent. This requires that NO_3^- be reduced to NO_2^- using nitrate reductase. Griess reagent is a mixture of equal volumes of 0.2% (w/v) naphthylenediamine and 0.2% (w/v) sulfanilamide prepared in 5% (v/v) phosphoric acid. The reagent was prepared freshly each time before use. Standard: 100 μmol Sodium nitrite stock solution was prepared and stored

at 4°C. Serial dilutions were carried out at the time of testing. 20–100 µmol/L of standard dilutions were prepared for testing NO₂ in plasma, and 0.5–2 µmol/L dilutions were prepared for the estimation of NO₂ in washed platelets suspensions. Plasma samples were brought to room temperature before starting the assay. Washed platelet suspensions were subjected to a series of freeze and thaw cycles and sonication to ensure complete platelet membrane disruption. Platelets suspensions and standard aliquots were incubated for 30 min at 37°C separately in tubes containing 0.2 U/mL nitrate reductase, 50 mmol HEPES buffer, 5 µM FAD, and 0.1 mmol NADPH in a total volume of 500 µL. Following incubation, 5 µL of 1 mmol potassium ferri-cyanide was added to each tube to oxidize any non-reacted NADPH, because reduced pyridine nucleotides (NADPH, NADH) strongly inhibit the Griess reaction. Samples were then incubated for an additional 10 min at 25°C. 1 mL of freshly prepared Griess reagent, then added to each tube, and the absorbance of each tube was determined at 543 nm, using a Syva S-111 spectrophotometer, from Gilford instrument Laboratories Inc., USA. Total nitrate and nitrite (µmol/L) were calculated from known standard concentrations.

Determination of nitric oxide synthase activity:

Nitric oxide synthase activity in washed platelets suspensions was determined by employing the reaction of NO with oxyhemoglobin, based on a modified method of Joan and Michael.¹⁹ NO reacts with oxyhemoglobin to form methemoglobin which absorbs at 401 nm. 50 µL of washed platelet suspension, 20 µL HEPES (100 mmol/L, pH 7.5), 40 µL H₄B (90 µmol/L) prepared in 100 mmol/L HEPES (pH 7.5) and dithiothreitol (100 mmol), 40 µL DL Valine (37 mmol/L), 10 µL CaCl₂ (6 mmol/L), and 10 µL MgCl₂ (30 mmol/L) were added using a microplate. The plate was incubated at 37°C for 10 min. 10 µL FAD (1.2 mmol/L), 20 µL NADPH (1.5 mmol/L) and 50 µL L-arginine (6 mmol/L) were then added, and the plate was further incubated for 15 min at 37°C. At the end of the incubation, the initial readings at 405 nm were immediately noted, and the increase in absorbance after 1, 2, and 3 min. was recorded. NOS activity in platelets was then calculated; the methemoglobin molar absorption coefficient is 60000 M⁻¹ cm⁻¹.

Determination of cyclic GMP: cGMP was measured in washed platelets suspensions using an enzyme immunoassay (EIA) commercial kit supplied by Biomedical Technologies Inc., USA, an assay based on a previous method of Honma et al.²⁰

Statistical analysis

Data were analyzed with computer software (S-plus 6 for Windows and SAS Software Release 8.2 packages). The results were expressed as mean ± SD, and the significance of the difference between the mean values of the groups were determined by the Student's t test employing the ANOVA program. Spearman's rank correlation was calculated to assess the association between the markers of NO-cGMP system and lipids or platelets function.

RESULTS

The subjects' age mean range was from 40–51 years. The study population has a small number of female enrollment, across all the groups.

There is a significant increase in serum total cholesterol and triglycerides ($P < 0.001$), in all CAD groups and a significant decreases in HDL ($P < 0.01$), compared to HC, the calculated LDL was significantly ($P < 0.001$) higher among the CAD groups compared to the controls.

Platelets counts were notably higher in CAD patients with UA or SA than in patients with MI or healthy controls. The differences between the means of platelets counts ($\times 10^9/L$ platelets) in HC Vs UA or SA are significant ($P < 0.01$). Platelets aggregation in the CAD patients groups and healthy controls increased immensely compared to platelets aggregation in healthy controls. The differences between the means of platelets aggregation (%) in MI, UA, or SA, patients and the healthy controls are greatly significant ($P < 0.001$). The respective means for the platelets aggregation (%) in HC, MI, UA and SA are 50.85 ± 10.76 , 70.95 ± 15.85 , 65.87 ± 20.16 , and 73.85 ± 16.67 . We also measured plasma-ionized calcium in all subjects. Abreast with the platelet aggregation; the plasma ionized Ca²⁺ levels in CAD patients and HC have demonstrated a similar trend. Plasma Ca²⁺ in CAD groups significantly increased ($P < 0.001$) compared to HC. The means ± SD of Ca²⁺ (mmol/L) in the study population were, 1.25 ± 0.19 , 1.41 ± 0.18 , 1.40 ± 0.14 , and 1.34 ± 0.15 for HC, MI, UA and SA respectively. The ionized Ca²⁺ levels in SA patients are slightly low compared to the remaining CAD groups; however, the differences between their means were not significant (Fig. 1).

Results of the various NO-cGMP system parameters studied in MI, UA, SA patients, and HC subjects are presented in Table 1. Plasma nitric oxide (NO) levels have increased significantly ($P < 0.001$) in MI and SA compared to HC, also increased in MI ($P < 0.001$) compared to the remaining CAD groups. However, the difference

Table 1 Platelets and plasma NO-cGMP variables

Groups/Variables (N = 40)	Plasma NO Mean $\pm$ SD $\mu\text{mol/L}$	Platelets NO Mean $\pm$ SD $\mu\text{mol}/10^9$ platelets	Platelets NOS Mean $\pm$ SD $\text{U}/10^9$ platelet	Platelets cGMP Mean $\pm$ SD $\text{Pmole}/10^9$ platelets
Healthy Controls	27.20 ± 8.92	1.47 ± 0.67	1.19 ± 0.56	0.95 ± 0.41
MI	56.75 ± 27.25	1.72 ± 0.60	1.21 ± 0.64	1.53 ± 0.64
Unstable Angina	31.22 ± 16.99	2.33 ± 0.83	1.64 ± 0.98	3.18 ± 0.77
Stable Angina	38.17 ± 17.69	2.25 ± 1.0	1.57 ± 0.81	5.12 ± 1.5
P	$P < 0.001$	$P < 0.001$	$P < 0.005$	$P < 0.001$

Table shows the levels of plasma NO, and platelets NO, cGMP, NO synthase activity in patients with CAD and healthy control.

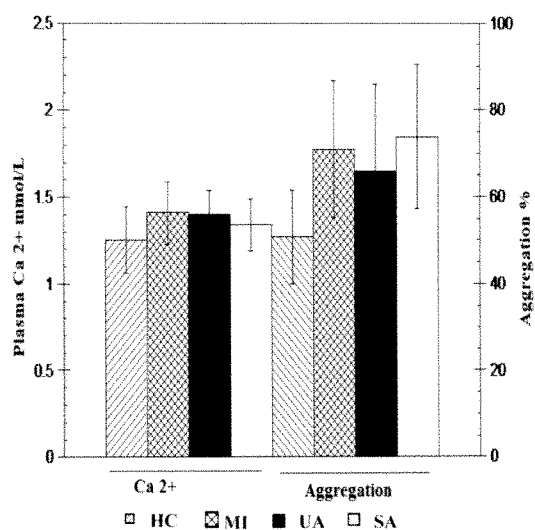


Fig. 1 Platelets aggregation and plasma Ca^{2+} levels in all groups. Plasma Ca^{2+} mmol/L (left) and platelet aggregation % (right) increases in CAD compared to HC, increases in Ca^{2+} may influence the platelet aggregation

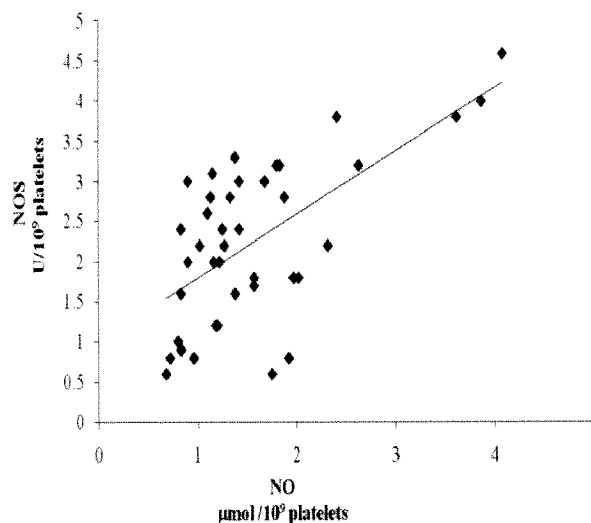


Fig. 2 NO- NOS levels in patients with stable angina. Platelet nitric oxide levels significantly correlated ($P < 0.0001$) with nitric oxide synthase activity ($r = 0.633$) in patients with stable angina.

between HC and UA is not significant. Platelets NO levels were significantly ($P < 0.001$) increased in UA and SA compared to HC or MI. The platelets NO levels, though increased in the MI group compared to HC; however, the difference was not statistically significant. Platelets NO correlated with platelets NO synthase activity ($r = 0.557$, $P < 0.001$), and cGMP ($r = 0.296$, $P < 0.05$). Platelet nitric oxide levels significantly correlated ($P < 0.0001$) with nitric oxide synthase activity ($r = 0.633$) in patients with stable angina (**Fig. 2**).

Platelets nitric oxide synthase activity levels in CAD patients and healthy controls were abreast with the NO-NO synthase activity trend. The NO synthase activity levels among the study groups were similar to that

depicted in platelets NO levels in CAD and HC groups; however, platelets NO synthase activity levels increased significantly in all CAD groups. The platelets cGMP levels in CAD patients and healthy controls as seen in **Table 1** have profoundly increased among CAD groups compared to HC ($P < 0.001$). Among the CAD groups, patients with SA have shown greater increases in platelets cGMP levels ($P < 0.001$), compared to the rest of the groups, likewise, cGMP levels in UA patients significantly ($P < 0.001$) increased compared to MI patients. Platelets cGMP levels correlated with platelets aggregation ($r = 0.461$, $P < 0.001$), and with platelets NOS activity ($r = 0.338$) in MI patients **Fig. 3**. Plasma ionized calcium (Ca^{2+}) explicitly increased ($P < 0.001$) in CAD groups compared to the healthy con-

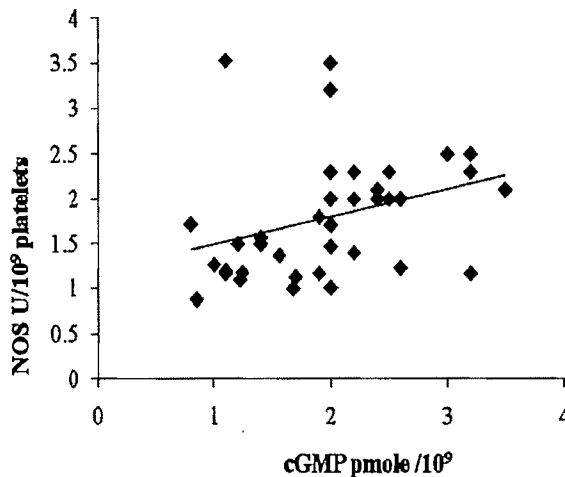


Fig. 3 NOS- cGMP in MI patients.

Platelets cGMP significantly correlated ($P < 0.001$) with Nitric oxide synthase activity ($r = 0.338$) in MI patients.

trols.

DISCUSSION

The major findings of this study are profound increases in NO-cGMP activity accompanied with increased Ca^{2+} levels in ischemic heart diseases. There is a paucity of data regarding NOS activity and the levels of platelet NO in CAD. There is no reported study to our knowledge, that compares the platelets NOS activity and NO levels among patients of CAD. There are several reports on NO levels in preeclampsia, hypertension, atherosclerosis, and heart failure showing a large spectrum of ambiguity on the subject. Experiments conducted in hypertensive animals have shown a similar diversity of findings, with NO generation reported to be normal, decreased, or enhanced.²¹⁻²⁹ Studies with reduced NO basal production in patients with essential hypertension were reported.^{30,31} The data were largely attributed to the reduced bio-activity of NO. Our results are in accordance with previously reported findings^{32,33}, however, in contradiction with the study of Minamino et al.,³⁴ whose observations suggested that the bio-availability of nitric oxide may decrease in patients exposed to multiple risk factors, and, therefore, contributing to myocardial ischemia and thrombotic vascular events. The discrepancy between the results of this study and that of others may be attributed to the fact that the plasma and platelets in this study were prepared from venous peripheral blood; however, other studies have focused either on plasma NO

levels taken from the femoral artery, spastic sites, or evaluated the basal NO release indirectly in the arterial and coronary sinus venous blood by the measurement of the blood flow velocity, oxygen saturation, and the endothelium dependent vasodilation, after infusion of NO donors and inhibitors.

Increased NO levels observed in the present study may support the hypothesis that increases in nitric oxide production may be a compensatory response to improve blood flow in the circulation, as suggested in a preeclampsia study mentioned earlier.²⁸ It is also possible that the increased NO levels may have been a response to increased platelet aggregation and adhesion in the circulation. In contrast, the increase in platelets NO levels demonstrated in this study could be due to the NO diffusion from the plasma, as it is reported that the released endothelial NO enters adjacent platelets and inhibits its activation.³⁵ Increased platelet NOS activity is noted in this study, and the significant correlation between platelet cGMP and platelets NO levels could provide a plausible explanation to the increased platelets NO, which may have resulted from the increased NOS activity in CAD (Fig. 3). In addition, the positive correlation between NOS and cGMP seen in MI patients can explain the differences between the three types of CAD episodes investigated in this study and may also indicate that the cGMP-NO system is activated at the initial stages of the disease. The turn on of the NO-NOS system during the initial stages of the disease may continue to compensate for the NO imbalance with the development of the disease as evident in the positive relationship between the NO-NOS that is seen in patients with stable angina. This may suggest an enhanced NO-cGMP system because of the increased NO basal release, in response to the elevated platelets activity and increased Ca^{2+} influx. The molecular mechanisms by which NO influences myocardial performance and platelets function are the subject of much investigation but remain largely unexplored. Much attention has been paid to cGMP pathways; the elevation of intra-platelet cGMP levels was suggested to mediate the anti-aggregating activity of exogenous and endogenous NO.³⁶ In platelets, cGMP inhibits agonist-induced increases in ionized Ca^{2+} ; this event could be a result of inhibition of both Ca^{2+} influx and Ca^{2+} mobilization and/or a result of stimulation of Ca^{2+} sequestration. An elevation in plasma ionized Ca^{2+} may have contributed to the increased platelets Ca^{2+} (data not shown) as earlier suggested³⁷ that the free calcium concentration in the extracellular fluid mediate and propagate the intracellular

Ca²⁺ influx. It has been hypothesized that the inhibition of Ca²⁺ influx by NO is secondary to its initial effects on sequestration of Ca²⁺ into the stores³⁸⁾; this agrees with the previous findings of Okamoto, et al.³⁹⁾ who studied the effects of NO on platelets Ca²⁺ inhibition.

The major strength of this study is the ability to control for a number of factors that influence platelets function, including antioxidants, vitamins, and other related drugs. A limitation of this study relates to its cross-sectional nature as we cannot determine whether the NO-cGMP system negatively influenced CAD or vice versa. In this analysis, we investigated the current NO-cGMP system markers in CAD, and these measurements may not be representative of the long-term NO status in platelets or endothelial cells. Longitudinal studies would better elucidate how the NO-cGMP system and CAD are related.

In conclusion, the present study demonstrated that the NO-cGMP signaling system concomitant Ca²⁺ fluxes profoundly enhanced in CAD. NO and cGMP though implicated previously in inhibiting Ca²⁺ influx, but seems to have an obscure or ancillary role to play to ameliorate the Ca²⁺ status, particularly in CAD patients. A further investigation is needed to elucidate distinctly the influence of NO-cGMP in Ca²⁺ platelet influx associated with CAD.

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REFERENCES

- 1) InterASIA Collaborative Group. Cardiovascular risk factor levels in urban and rural Thailand—The International Collaborative Study of Cardiovascular Disease in Asia (InterASIA). *Eur J Cardiovasc Prev Rehabil* 2003; **10**: 249–57.
- 2) Parthasarathy S, Litvinov D, Selvarajan K, Garelnabi M. Lipid peroxidation and decomposition—conflicting roles in plaque vulnerability and stability. *Biochim Biophys Acta* 2008; **1781**: 221–31.
- 3) Libby P. Inflammation and cardiovascular disease mechanisms. *Am J Clin Nutr* 2006; **83**: 456S–60S.
- 4) Levonen AL, Inkala M, Heikura T, Jauhiainen S, Jyrkkanen HK, Kansanen E, et al. Nrf2 gene transfer induces antioxidant enzymes and suppresses smooth muscle cell growth in vitro and reduces oxidative stress in rabbit aorta in vivo. *Arterioscler Thromb Vasc Biol* 2007; **27**: 741–7.
- 5) Gkaliagkousi E, Ritter J, Ferro A. Platelet-derived nitric oxide signaling and regulation. *Circ Res* 2007; **101**: 654–2.
- 6) Lai H, Aronow W, Rachdev A, Asija A, Lai K, George J, et al. Incidence of mortality in 1,040 patients with coronary heart disease or hypertensive heart disease with normal and abnormal left ventricular ejection fraction and with normal and abnormal QRS duration. *Arch Med Sci* 2008; **4**: 140–2.
- 7) Watala C, Chudzik A, Tchorezewski H, Gwozdziński K. Impaired action of nitric oxide on blood platelets in premature newborns. *Arch Med Sci* 2008; **3**: 315–23.
- 8) Antoniadou C, Shirodaria C, Van Assche T, Cunningham C, Tegeder I, Lotsch J, et al. GCH1 haplotype determines vascular and plasma biopterin availability in coronary artery disease effects on vascular superoxide production and endothelial function. *J Am Coll Cardiol* 2008; **52**: 158–65.
- 9) Petidis K, Douma S, Doumas M, Basagiannis I, Vogiatzis K, Zamboulis C. The interaction of vasoactive substances during exercise modulates platelet aggregation in hypertension and coronary artery disease. *BMC Cardiovasc Disord* 2008; **8**: 11.
- 10) Joseph S, Beckman W, Koppeno I. Nitric oxide, Superoxide, and Peroxynitrite: The good, the bad, and the ugly. *Am J Physiol* 1996; **271**: C1427–C37.
- 11) Popescu I, Panoiu C, Hinescu M, Nutu O. The mechanism of cGMP-induced relaxation in vascular smooth muscle. *Eur J Pharmacol* 1985; **107**: 393–4.
- 12) Navarro-Dorado J, Orensanz LM, Recio P, Bustamante S, Benedito S, Martínez AC, et al. Mechanisms involved in testosterone-induced vasodilatation in pig prostatic small arteries. *Life Sci* 2008; **8**: 569–73.
- 13) O'Donnell M, Owen E. Atrial natriuretic factor stimulates Na/K/Cl cotransport in vascular smooth muscle cells. *Proc Natl Acad Sci USA* 1986; **83**: 6132–6.
- 14) Wu YZ, Li SQ, Zu XG, Du J, Wang FF. Ginkgo biloba extract improves coronary artery circulation in patients with coronary artery disease: contribution of plasma nitric oxide and endothelin-1. *Phytother Res* 2008; **22**: 734–9.
- 15) The Criteria Committee of the New York Heart Association. Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Great Vessels. 9th ed. Boston, Mass: Little, Brown & Co, 1994.
- 16) Sir John V, and Lewis S. (1991): Practical Haematology. 7th Ed. pp. (55–56a) and (293–318b). Medical Division of Longman Group (Churchill Livingstone) UK.
- 17) Fraser J, Raelene L, Marian A. Isolation of human platelets from plasma by centrifugation and washing. *Methods Enzymol* 1989; **169**: 3–10.
- 18) Grisham MB, Johnson GG, Lancaster JR. Quantitation of nitrate and nitrite in extracellular fluids. *Methods Enzymol* 1996; **268**: 237–46.
- 19) Joan H, Michael M. Nitric-Oxide synthase assays. *Methods Enzymol* 1994; **233**: 250–8.
- 20) Honma M, Satoh T, Takezawa J, Ui M. An ultrasensi-

- tive method for the simultaneous determination of cyclic AMP and cyclic GMP in small-volume samples from blood and tissue. *Biochem Med* 1977; **18**: 257–73.
- 21) Kuga T, Egashira K, Mohri M, Tsutsui H, Harasawa Y, Urabe Y, et al. Bradykinin-induced vasodilation is impaired at the atherosclerotic site but is preserved at the spastic site of human coronary arteries in vivo. *Circulation* 1995; **92**: 183–9.
 - 22) Leaf C, Winshnok J, Tannenbaum S. L-arginine is precursor of nitrate biosynthesis in humans. *Biochem Biophys Res Commun* 1989; **163**: 1032–7.
 - 23) Kaufmann PA, Rimoldi OE, Gneccchi-Ruscione T, Luscher TF, Camici PG. Systemic nitric oxide synthase inhibition improves coronary flow reserve to adenosine in patients with significant stenoses. *Am J Physiol Heart Circ Physiol* 2007; **293**: H2178–82.
 - 24) Lyall F, Young A, Greer IA. Nitric oxide concentrations are increased in the fetoplacental circulation in preeclampsia. *Am J Obstet Gynecol* 1995; **173**: 714–8.
 - 25) Wu Y, Li S, Cui W, Zu X, Wang F, Du J. Ginkgo biloba extract improves coronary blood flow in patients with coronary artery disease: role of endothelium-dependent vasodilation. *Planta Med* 2007; **73**: 624–8.
 - 26) Cachofeiro V, Nasjletti A. Increased vascular responsiveness to bradykinin in kidneys of spontaneously hypertensive rats. Effect of N omega-nitro-L-arginine. *Hypertension* 1991; **18**: 683–8.
 - 27) Yamazaki J, Fujita N, Nagao T. NG-monomethyl-L-arginine-induced pressor response at developmental and established stages in spontaneously hypertensive rats. *J Pharmacol Exp Ther* 1991; **259**: 52–7.
 - 28) Koller A, Huang A. Impaired nitric oxide-mediated flow-induced dilation in arterioles of spontaneously hypertensive rats. *Circ Res* 1994; **74**: 416–21.
 - 29) Malte K, Martin F, Thomas K, Andreas D, Wolfgang M, Bodo E. Role of nitric oxide in the regulation of coronary vascular tone in hearts from hypertensive rats. Maintenance of nitric oxide-forming capacity and increased basal production of nitric oxide. *Hypertension* 1995; **25**: 186–93.
 - 30) Node K, Kitakaze M, Yoshikawa H, Kosaka H, Hori M. Reduced plasma concentrations of nitrogen oxide in individuals with essential hypertension. *Hypertension* 1997; **30**: 405–8.
 - 31) Ilhan N, Seckin D, Ilhan N, Ozbay Y. Abnormal asymmetric dimethylarginine/nitric oxide balance in patients with documented coronary artery disease: relation to renal function and homocysteine. *J Thromb Thrombolysis* 2007; **23**: 205–11.
 - 32) Komori K, Matsumoto T, Ishida M, Kuma S, Yone-mitsu Y, Eguchi D, et al. Enhancement of nitric oxide production after arterial reconstruction in patients with arteriosclerosis obliterans. *J Vasc Surg* 1997; **26**: 657–2.
 - 33) Rudolph V, Steven D, Gehling UM, Goldmann B, Rudolph TK, Friedrichs K, et al. Coronary plaque injury triggers neutrophil activation in patients with coronary artery disease. *Free Radic Biol Med* 2007; **42**: 460–5.
 - 34) Minamino T, Kitakaze M, Sato H, Asanuma H, Funaya H, Koretsune Y, et al. Plasma levels of nitrite/nitrate and platelet cGMP levels are decreased in patients with atrial fibrillation. *Arterioscler Thromb Vasc Biol* 1997; **17**: 3191–5.
 - 35) Naseem K, Susanna C, Mohammadi B, Richard B. The synergism of hydrogen peroxide with plasma S-nitrosothiols in the inhibition of platelet activation. *Biochem J* 1996; **318**: 759–66.
 - 36) Radomski W, Palmer J, Moncada S. The role of nitric oxide and cGMP in platelet adhesion to vascular endothelium. *Biochem Biophys Res Commun* 1987; **148**: 1482–9.
 - 37) Krassimira I, Michael S, Chrisian D, Rupert G. Effect of nitric oxide-containing compounds on increases in cytosolic ionized Ca^{2+} and on aggregation of human platelets. *Eur J Pharmacol* 1993; **244**: 37–47.
 - 38) Cheung Y, Bonaventura V, Malis D, Leaf A. Calcium and ischemic injury. *N Engl J Med* 1986; **314**: 1670–6.
 - 39) Okamoto Y, Ninomiya H, Miwa S, Masaki T. Capacitative Ca^{2+} entry in human platelets is resistant to nitric oxide. *Biochem Biophys Res Commun* 1995; **212**: 90–6.

► **Original Article** ◀

Ultrasonographic Character of Carotid Plaque and Postprocedural Brain Embolisms in Carotid Artery Stenting and Carotid Endarterectomy

Hiroshi Mitsuoka, MD, PhD,¹ Tsunehiro Shintani, MD, PhD,¹ Hidekazu Furuya, MD, PhD,²
Yoshinaga Nakao, MD, PhD,² and Shigeki Higashi MD, PhD²

Objective: To investigate ultrasonographic character of carotid plaques, and incidences of brain embolism in carotid angioplasty and stenting (CAS) and carotid endarterectomy (CEA).

Materials and Methods: CEA (22/25 symptomatic lesions) and CAS (17/20 symptomatic lesions) between 2007 and 2010. Embolic protection devices (15 occlusion and 5 filtering devices) were used during CAS. Carotid plaques were classified into three categories (I: calcificated, II: intermediately echogenic, III: echolucent). Magnetic resonance imaging (MRI) was used to investigate brain emboli.

Results: Ultrasonographic character of the plaques in CEA cases (I: 4%, II: 88%, III: 8%) was different from the one in CAS cases (I: 10%, II: 90%, III: 0%). The incidence of brain embolism in the CAS cases was 52.6 % while 0% in the CEA cases ($p = 0.00037$). CAS had high incidences of brain embolism in any plaques (I: 100%, II: 43.8%). In the most recent 9 procedures of CAS using occlusion devices, averaged number of embolic lesion was 1.0 (0 post operative day; 0 POD). The number increased as 1.4 (1 POD) and 2.0 (7 POD).

Conclusion: CEA should be currently the first choice for most patients with a high-grade and symptomatic carotid artery stenosis.

Key words: carotid endarterectomy, carotid angioplasty, brain embolism, diffusion-weighted magnetic resonance imaging, carotid plaque

INTRODUCTION

Carotid angioplasty (CAS) emerged as an alternative treatment for carotid artery stenosis for carotid endarterectomy (CEA) to prevent neurological ischemic events. Ironically, one of the frequent complications in these invasive procedures is brain infarction, most of

which are caused by embolic particles from carotid plaques. Especially, ultrasonographic frequency of embolic events in CAS is significantly higher than in CEA.¹⁾ The release of embolic materials may be related to the character of culprit plaques.²⁾ In the present study, we investigated ultrasonographic character of carotid plaques (i.e. echolucent, intermediately echogenic, and calcificated), and embolic events in CEA and CAS using diffusion-weighted magnetic resonance imaging (DW-MRI). The incidence of brain emboli was calculated in each category of ultrasonographic character, and safety and efficacy of both invasive procedures were evaluated.

MATERIALS AND METHODS

Between July 2007 and May 2010, 25 and 20 procedures of CEA and CAS were performed in our hospital.

¹Department of Vascular Surgery, Shizuoka Red Cross Hospital, Shizuoka, Shizuoka, Japan

²Department of Cardiac Surgery, Shizuoka Red Cross Hospital, Shizuoka, Shizuoka, Japan

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Corresponding author: Hiroshi Mitsuoka, Department of Vascular Surgery, Shizuoka Red Cross Hospital, 8-2 Ote-machi, Aoi-ward, Shizuoka, Shizuoka 420-8630, Japan

Tel: +81-54-254-4311, Fax: +81-54-272-6983

E-mail: mitsuoka@SZRC.org

Before the treatments, all culprit lesions were examined by ultrasonography, and the plaques were categorized into three categories. Category I indicates the lesion with a highly calcified plaque, II intermediately echogenic, and III echolucent. CAS and CEA were indicated for symptomatic carotid lesions (at least 3 weeks after the most recent infarction, transient ischemic attack) and asymptomatic high-grade stenotic lesions ($\geq 80\%$ by NASCET method³⁾). CEA was performed on 22 symptomatic lesions, or and 3 asymptomatic lesions, with a high-grade stenosis (70%–97%, MEAN 91.7%), while CAS on 17 symptomatic and 3 asymptomatic lesions (80%–97%, MEAN 89.5 %).

Basically, CAS was indicated for CEA high-risk cases (19 out of 20 lesion), as defined by SAPHIRE inclusion criteria.⁴⁾ In one case, although the patient had an ipsi-lateral radiation therapy for laryngeal cancer, the lesion with an echo-lucent plaque was treated by CEA. Embolic protection was performed using an occlusion balloon (Percu Surge, Medtronic, Santa Rosa, CA) in 15 CAS cases, or a filtering device (AngioGuard™ XP, Cordis Corporation, Johnson and Johnson, Miami, FL) in 5 of CAS cases. A closed cell type stent (Wallstent, Boston Scientific Corporation, Boston, MA) was used in combination with the occlusion balloon, while an open cell type stent (Precise, Cordis Corporation, Johnson and Johnson, Miami, FL) was used with the filtering device.

All patients were examined by neurologists pre- and post-procedurally. Pre- and post-procedural DW-MRIs were performed to investigate the postprocedural brain emboli within a post-procedural week, using Signa Horizon (GE health care, Japan), at the settings of TR/TE = 1000/135 milliseconds, b factor = 1500, 6 mm thick slice, 2 mm gap, and matrix size 128 × 128. An acute ischemic lesion was diagnosed when it was seen on DW-MRI images. To be considered indicative of acute injury, the lesion could not appear on pre-procedural imaging, and no corresponding FLAIR abnormality could be present for the lesion to be considered as acute.

The temporal distribution pattern of the post-procedural embolism was examined in the most recent 9 procedures of CAS using an occlusion balloon for embolic protection and a closed cell type stent, using the results of repeated MRIs performed at either two of the following time-points; 0 post operative day (0 POD; 4 procedures), 24–48 hours (1 POD; 7 procedures), and a week after the procedure (7 POD; 5 procedures). The time points of consecutive MRIs were decided by the availability of MRI facility in our hospital. Thus, MRIs were

available at 0 POD and 1POD (3 cases), 0 POD and 7 POD (1 case), and 1 POD and 7 POD (5 cases). For statistical analysis, Kai-square method and t-test were used if applicable.

RESULTS

Neurological findings in the 30 postprocedural days

One patient (5%) in the CAS group had ipsi-lateral reversible ischemic nerve damage, while one patient (4%) in the CEA group had a contra-lateral brain hemorrhage from brain metastasis of bladder cancer on the third postoperative day. Myocardial infarction, death, or cranial nerve injury was not experienced in these treatments.

Postprocedural brain emboli detected by DW-MRI

Incidence of brain embolism in the CAS case was 50.0 %. On the other hand, DW-MRI detected no brain emboli in the CEA cases ($p = 0.00037$).

Temporal distribution pattern of the postprocedural embolism

The number of embolic lesion detected by MRI at <3 h was 1.0 on average. The number increased as 1.4 and 2.0, at 1 POD and 7 POD.

Sonographic categories and brain emboli

Constitution of ultrasonographic character of the plaques in CEA cases (I: 4%, II: 88%, III: 8%) was different from the one in CAS cases (I: 10%, II: 90%, III: 0%). CEA procedures resulted in 0 percent incidences of brain emboli, even in the cases of echo-lucent and risky plaques. On the other hand, CAS had high incidences of brain emboli in any ultrasonographic characters of plaques (I: 100%, II: 43.8%) (Fig. 1).

DISCUSSION

DW-MRI revealed that CAS caused micro-brain emboli (MBE) in half of the cases, although similar neurological results were provided to those of CEA. Because of the limited number of the cases, there may be an effect of a learning curve, which may decrease the embolic events in CAS cases. However, considering a high percentage of symptomatic cases involved (85%), the frequency of MBE did not seem significantly higher than the one in a larger scale study.⁵⁾

Symptomatic and asymptomatic carotid plaques seem to have considerably different pathophysiological charac-

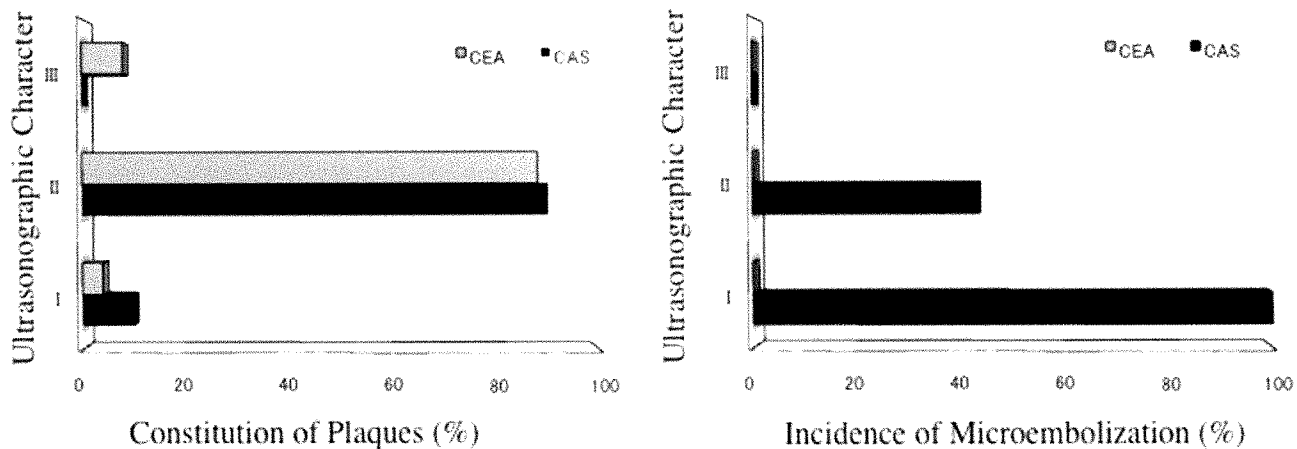


Fig. 1 Sonographic categories and postprocedural brain emboli.

Left: Constitution of ultrasonographically categorized lesion in each treatment group.

Right: Incidences of brain micro-emboli in CAS or CEA were separately shown in each category. Category I indicates the lesion with a highly calcified plaque, II intermediately echogenic, and III echolucent.

CAS, carotid angioplasty and stenting; CEA, carotid endarterectomy

ters. More or less, symptomatic carotid lesions can be considered to have such unfavorable features, that releases embolic particles when activated by unknown mechanisms. In fact, embolic events are ultrasonographically detected more frequently in patients with recent neurological symptoms, compared with patients having similarly high grades but asymptomatic carotid plaques.^{6, 7)} During the CAS procedures, direct contact of the devices with such vulnerable lesions inevitably influences the release of plaque fragments. Moreover, as detected in this series, CAS leaves the atheromatous plaque, which may cause post-procedural emboli.⁵⁾ Thus, not only the usage of per-procedural embolic protection devices, but also understanding the pathophysiological character of the plaques is essential to improve the results of carotid intervention. We did not treat the cases with echolucent plaques with CAS, because it suggests the instability of the culprit lesion and a "CAS high-risk" character, such as lipid rich core in the plaque or newly formed thrombus.⁸⁾

Hypothesizing the outcomes of CAS is strongly influenced by the characters of plaques, our results suggested that applying CAS for all of these CEA cases would have made a similarly high incidence of brain emboli in the group II. Furthermore, a higher incidence of symptomatic emboli might have been detected in the cases with echolucent plaques (group III). Regarding asymptomatic emboli, there is a report indicating that the cognitive faculties in a great number of these "asymptomatic" patients

are decreased.⁹⁾ Recently published large trials have shown that the mid-term results of CAS were not extremely inferior, but apparently not superior to CEA, especially in terms of preventing new strokes.^{10, 11)} However, if we indicate CEA for all these CAS cases, there should have been high incidences of complications, including cranial nerve injuries, MI, and even death.

There are limitations in interpreting the results of this study. As afore mentioned, the small number of cases in the current study may have some effects on the results. Furthermore, the results of two different procedural protocols were involved in the CAS cases, mainly due to the availability of devices. However, we detected 2 cases of brain emboli in 5 procedures using an open cell type stent and a filtering device, while 8 in 15 using an occlusion balloon and a closed cell type stent. Therefore, the differences in device seemed to have a small effect on the results.

In conclusion, CEA should be currently the first choice for most patients with a high-grade and symptomatic carotid artery stenosis. CAS should be reserved for the case with such high CEA risks that the expected incidence of brain embolism is reasonably accepted.

REFERENCES

- 1) Biasi GM, Froio A, Diethrich EB, Deleo G, Galimberti S, Mingazzini P, et al. Carotid plaque echolucency increases the risk of stroke in carotid stenting:

- the Imaging in Carotid Angioplasty and Risk of Stroke (ICAROS) study. *Circulation* 2004; **110**: 756-62.
- 2) Ohki T, Marin ML, Lyon RT, Berdejo GL, Soundararajan K, Ohki M, et al. Ex vivo human carotid artery bifurcation stenting: correlation of lesion characteristics with embolic potential. *J Vasc Surg* 1998; **27**: 463-71.
 - 3) North american symptomatic carotid endarterectomy trial collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade stenosis. *N Engl J Med* 1991; **325**: 445-53.
 - 4) Yadav JS, Wholey MH, Kuntz RE, Fayad P, Katzen BT, Mishkel GJ, et al. Protected carotid-artery stenting versus endarterectomy in high-risk patients. *N Engl J Med* 2004; **351**: 1493-501.
 - 5) Rapp JH, Wakil L, Sawhney R, Pan XM, Yenari MA, Glastonbury C, et al. Subclinical embolization after carotid artery stenting: New lesions on diffusion-weighted magnetic resonance imaging occur postprocedure. *J Vasc Surg* 2007; **45**: 867-74.
 - 6) Sitzler M, Muller W, Siebler M, Hort W, Kniemeyer HW, Jancke L, et al. Plaque ulceration and lumen thrombus are the main sources of cerebral microemboli in high-grade internal carotid artery stenosis. *Stroke* 1995; **26**: 1231-3.
 - 7) Markus HS, Thomson ND, Brown MM. Asymptomatic cerebral embolic signals in symptomatic and asymptomatic carotid artery disease. *Brain* 1995; **118**: 1005-11.
 - 8) Saam T, Ferguson MS, Yarnykh VL, Takaya N, Xu D, Polissar NL, et al. Quantitative evaluation of carotid plaque composition by in vivo MRI. *Arterioscler Thromb Vasc Biol* 2005; **25**: 234-9.
 - 9) Gossetti B, Gattuso R, Irace L, Faccenna F, Venosi S, Bozzao L, et al. Embolism to the brain during carotid stenting and surgery. *Acta Chir Belg* 2007; **107**: 151-4.
 - 10) Brott TG, Hobson RW 2nd, Howard G, Roubin GS, Clark WM, Brooks W, et al. Stenting versus endarterectomy for treatment of carotid-artery stenosis. *N Engl J Med* 2010; **363**: 11-23.
 - 11) International Carotid Stenting Study investigators, Ederle J, Dobson J, Featherstone RL, Bonati LH, van der Worp HB, et al. Carotid artery stenting compared with endarterectomy in patients with symptomatic carotid stenosis (International Carotid Stenting Study): an interim analysis of a randomised controlled trial. *Lancet* 2010; **375**: 985-97.

» Original Article «

CHADS2 Score is a Poor Predictor of Non-cerebral Acute Arterial Occlusion in Patients with Non-valvular Atrial Fibrillation

Kota Yamamoto, MD, PhD,¹ Tadashi Kitaoka, MD,¹ Harunobu Matsumoto, MD,¹ Juno Deguchi, MD, PhD,¹ Michio Shiibashi, PhD,² and Osamu Sato, MD, PhD¹

Objective: The CHADS2 score is a stroke risk stratification scheme in patients with non-valvular atrial fibrillation (NVAF). The aim of this study was to determine whether the CHADS2 score can help to predict the risk of non-cerebral acute arterial embolism.

Materials and Methods: One hundred and seventeen patients who underwent surgery for non-cerebral acute arterial embolism with NVAF between 1997 and 2009 were enrolled in the cross sectional study. The CHADS2 score of each patient was calculated at the onset of symptoms. The distribution of the CHADS2 score was compared with that of other studies analyzing patients with stroke.

Results: The perioperative mortality was 11.1%. A comparison of patients with stroke revealed that our distribution curves were significantly shifted to the left, showing that the CHADS2 score did better in predicting stroke than non-cerebral embolism. On the other hand, the distribution in our series coincides with that of NVAF patients in general. These results indicated that the risk of non-cerebral embolism occurs at the same rate regardless of the CHADS2 score.

Conclusions: The CHADS2 scoring system seems to be an unreliable predictor of non-cerebral embolism, and may not contribute in avoiding potentially life-threatening acute arterial occlusion of the peripheral artery.

Key words: CHADS2 score, non-cerebral embolism, non-valvular atrial fibrillation, anticoagulation

INTRODUCTION

Non-valvular atrial fibrillation (NVAF) is prevalent in 1% of the general population, and its prevalence increases with age.^{1, 2)} Thromboembolic events comprise one of the most important factors affecting the prognosis of patients with NVAF, and annual stroke rates are re-

ported to range between 2% to 10%.^{3–6)} Although these thromboembolic events can occur in cerebral, mesenteric and peripheral arteries of the limbs, many studies have concentrated on stroke. Acute occlusion of the mesenteric or peripheral arteries can also be life threatening, and if not fatal, can lead to short bowel syndrome or limb loss that could reduce the quality of life of patients who survive these events.

The CHADS2 score has been proposed and validated as a straightforward and practical stratification of the risk of stroke in patients with NVAF.⁷⁾ Since then, the CHADS2 score has been advocated as the means to determine anticoagulation needs in patients with NVAF, but to our knowledge, a scoring system for non-cerebral acute arterial occlusion has not been established.^{8, 9)} The present study thus aimed to determine whether the CHADS2 score can help to predict the risk

¹Department of Vascular Surgery, Saitama Medical Center, Saitama Medical University, Kawagoe, Saitama, Japan

²Information Technology Center, Saitama Medical University, Moroyama-cho, Saitama, Japan

Received: January 4, 2011; Accepted: April 1, 2011
Corresponding author: Kota Yamamoto, MD, PhD. Department of Vascular Surgery, Saitama Medical Center, Saitama Medical University, 1981 Kamoda, Kawagoe, Saitama 350-0844, Japan
Tel: +81-49-228-3462, Fax: +81-49-228-3462
E-mail: k-yamamo@tc4.so-net.ne.jp

Table 1 Characteristics of patients according to location of embolism

	Overall (n = 117)	Upper limb (n = 18)	Lower limb (n = 89)	Mesenteric (n = 10)
Mean age $\pm$ SD	75.8 $\pm$ 10.9	81.8 $\pm$ 9.3	75.4 $\pm$ 10.8	69.1 $\pm$ 11.3
Male/Female	76/41	10/8	60/29	6/4
CHF	17 (14.5%)	2 (11.1%)	14 (15.7%)	1 (10.0%)
HT	38 (32.4%)	7 (38.9%)	27 (30.3%)	4 (40.0%)
Age	61 (52.1%)	13 (72.2%)	44 (49.4%)	4 (40.0%)
DM	31 (26.4%)	1 (5.6%)	27 (30.3%)	3 (30.0%)
Stroke	32 (27.4%)	6 (33.3%)	24 (27.0%)	2 (20.0%)
CHADS2 score	1.8 $\pm$ 1.3	1.9 $\pm$ 1.4	1.8 $\pm$ 1.3	1.6 $\pm$ 0.8
Perioperative death	13 (11.1%)	0 (0%)	10 (11.2%)	3 (30.0%)

SD, standard deviation; CHF, congestive heart failure; HT, hypertension; DM, diabetes mellitus

of non-cerebral acute arterial embolism in patients with NVAf by comparing the outcomes with those of studies of cerebral thromboembolic events.

MATERIALS AND METHODS

This study proceeded according to the guidelines of the research ethics committee of our institution and enrolled 117 patients who underwent surgery for non-cerebral acute arterial embolism with atrial fibrillation between 1997 and 2009. Patients with valvular disease or aneurysm of the peripheral artery were excluded using echocardiograms and vascular ultrasonography. We retrospectively calculated CHADS2 scores at the time of admission as chronic heart failure (treatment or diagnosis of congestive heart failure within 1 year), hypertension (under medication or with systolic blood pressure of ≥ 160), age (≥ 75 years), diabetes (diagnosed and treated as diabetic or with HbA1C of $\geq 6\%$), stroke (history of stroke or transient ischemic attack).

The results were analyzed and compared with others.^{1, 10, 11} The distribution of patients in each CHADS2 score category was compared using the χ^2 test. A P value of <0.05 was considered significant. All data were analyzed using JMP 5.0 software (SAS Institute Inc.).

RESULTS

Among 117 patients, 18, 89 and 10 had embolism of the upper limb, lower limb and mesenteric artery, respectively. **Table 1** shows the baseline characteristics of patients enrolled in the study. Patients with upper limb embolism were significantly older.

Only 13 patients were receiving anticoagulation ther-

Table 2 Number of patients in each CHADS2 score group (n = 117)

CHADS2 score	Number of patients
0	16 (13.7%)
1	44 (37.6%)
2	21 (17.9%)
3	22 (18.8%)
4	11 (9.4%)
5	3 (2.6%)
6	0 (0.0%)

apy upon arrival at the hospital, and only two were within the therapeutic range (INR >2.0). In addition, 24 patients were under antiplatelet therapy. The main reason for a low proportion of patients under anticoagulation seemed to be that NVAf was not detected until the embolic episode.

Ninety-four patients underwent thromboembolectomy alone, seven underwent bypass surgery for lower limb, five underwent bowel resection with or without embolectomy, eight underwent primary amputation and three were unable to undergo surgery due to their concomitant medical problems. In our institution, we try bypass surgery for acute arterial occlusion of the lower limb when (1) thromboembolectomy was unsuccessful, (2) good outflow artery was confirmed preoperatively, and (3) the risk of reperfusion syndrome seemed low. The perioperative mortality within 30 days of the operation was 11.1%. The mortality rate in the group with mesenteric artery occlusion was significantly high (30.0%).

Table 2 shows the numbers and proportions of patients in each CHADS2 score group. We then compared our results with those of two studies in the United States of

Table 3 Comparison of the present and other findings of patients with stroke

Authors	CHADS2 score				P value (vs. present study)
	0	1–2	3–4	5–6	
Rietbrock ¹⁾ (n = 5526)	161	2026	2598	741	<0.0001
Gage ⁶⁾ (n = 94)	2	40	44	8	0.0002
Masaki ⁷⁾ (n = 23)	1	9	12	1	Not available*
Present study (n = 117)	16	65	33	9	

* Not available due to small number of patients.

Table 4 Comparison of the present and other findings of non-valvular atrial fibrillation

Authors	CHADS2 score				P value (vs. present study)
	0	1–2	3–4	5–6	
Rietbrock ¹⁾ (n = 51807)	6686	31351	12086	1684	0.61
Gage ⁶⁾ (n = 1733)	120	986	557	70	0.08
Masaki ⁷⁾ (n = 265)	39	158	65	3	0.64
Present study (n = 117)	16	65	33	9	

America and one in Japan reports regarding stroke and CHADS2 scores.

We firstly compared the present series with reported cohorts who had a stroke. **Figure 1** and **Table 3** show the proportions of patients in each CHADS2 score category. Although we found no significant differences compared with the results of Masaki,¹¹⁾ a comparison with the other two studies revealed that our curves were significantly shifted to the left, whereas those in the reports were almost identical. This meant that the risk of non-cerebral occlusion was high even in patients with a low CHADS2 score, a group of patients regarded to have a low risk for stroke. This shifting of the curve to the left indicates that CHADS2 scores can more accurately predict the likelihood of stroke than non-cerebral embolism.

We then compared our results with those from all patients with NVAF in general. **Figure 2** and **Table 4** show that the CHADS2 score distribution in our series coincides with that of NVAF patients in general. These results indicated that the risk of non-cerebral embolism occurs at the same rate regardless of the CHADS2 score.

DISCUSSION

Thromboembolic events, especially stroke, probably comprise an important factor affecting the prognosis of patients with NVAF.¹²⁾ The main preventive therapy is anticoagulation, and Fitzmaurice reported that warfarin decreases the rate of death by 33% and the rate of the combined outcome of stroke, systemic embolism, or death by 48%.⁸⁾ The main difficulty with anticoagulation therapy is its adverse effect of causing a bleeding tendency. This inevitably invoked the question of who is likely to benefit the most from anticoagulation therapy and who is not. To overcome these issues, CHADS2 scores have been proposed in the West and Japan as a means of assessing the risk of stroke in patients with NVAF.^{7, 9, 11)}

Although CHADS2 scores play a significant role in predicting stroke, no studies have demonstrated whether it can predict other types of acute arterial occlusion such as that of the arteries of the upper and lower limbs and abdominal organs. Acute ischemia of the lower limb and

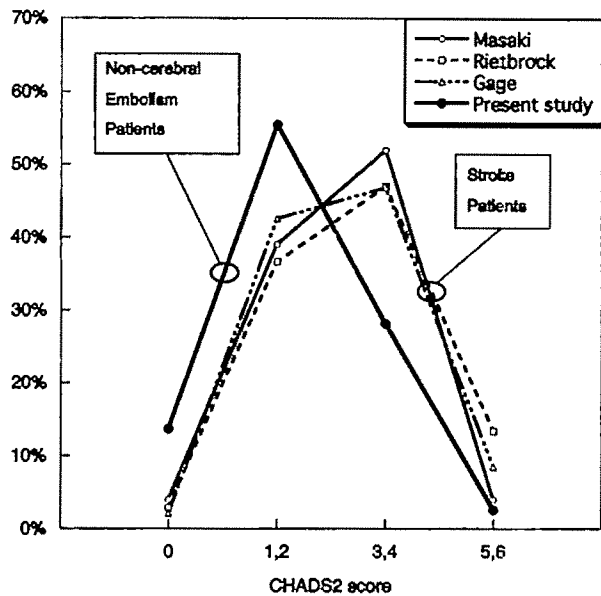


Fig. 1 Proportion of patients with arterial occlusive symptoms in each CHADS2 score category.

Non-cerebral arterial occlusion is the symptom in present study and stroke is the symptom in the other three studies. Compared with stroke, patients with a lower CHADS2 score are at high risk of non-cerebral peripheral embolism.

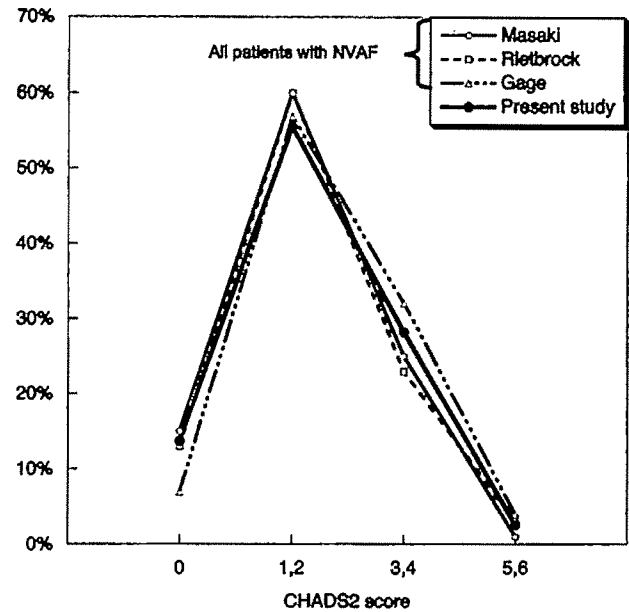


Fig. 2 Comparison of our series with proportion of all patients with NVAF in each CHADS2 score category of the remaining three studies.

The distribution of the CHADS2 score of the present series coincides that of general population with NVAF.

NVAF, non-valvular atrial fibrillation

abdominal organs can also be fatal.^{13, 14)}

The aim of this study was to determine whether and how much the CHADS2 score could predict the risk of non-cerebral acute arterial embolism. We compared our results with data from other studies of the risk of stroke using the CHADS2 score.^{1, 10, 11)}

Because the CHADS2 score includes stroke as an important factor, it obviously predicted stroke more accurately than other types of arterial occlusions (**Fig. 1**). However, it had little or no predictive value for non-cerebral embolism (**Fig. 2**). One of the main points of the CHADS2 score is that, patients with a low score have a low risk for stroke and anticoagulation therapy helps little to improve the stroke rate. However, our result points out that the prevalence of non-cerebral arterial embolism is not at all lower compared with the higher score group, and anticoagulation therapy should be the same regardless of the score.

The present retrospective study has some limitations. Because we analyzed data only from patients with symptomatic embolism, we had to postulate that patients with NVAF had similar characteristics (CHADS2 score proportion, risk for embolism, etc.) to those reported by others.

The reason why the CHADS2 score had a poor prediction rate for non-cerebral occlusion remains unclear. One difference between cerebral and non-cerebral occlusion seems to be the size of the embolus required to elicit symptoms. We postulate that the CHADS2 score would be more effective in predicting the production of small emboli.

Regardless of the reason, no tools can yet predict non-cerebral arterial embolism in patients with NVAF. Rietbrock also stated that although the CHADS2 score is a good predictor of stroke risk, it could still be improved.⁹⁾ Until another tool for detecting non-cerebral occlusion is developed, all patients with NVAF should undergo anticoagulation therapy unless contraindicated (high risk of falls, history of peptic ulcers etc.).

CONCLUSION

The CHADS2 scoring system seems to be an unreliable predictor of non-cerebral embolism, and anticoagulation therapy according to the CHADS2 score might not avoid potentially life-threatening acute arterial occlusion of the peripheral artery. Therefore, we propose that all patients with NVAF should be anticoagulated, unless contraindicated.

REFERENCES

- 1) Rietbrock S, Heeley E, Plumb J, van Staa T. Chronic atrial fibrillation: Incidence, prevalence, and prediction of stroke using the Congestive heart failure, Hypertension, Age >75, Diabetes mellitus, and prior Stroke or transient ischemic attack (CHADS2) risk stratification scheme. *Am Heart J* 2008; **156**: 57-64.
- 2) Feinberg WM, Blackshear JL, Laupacis A, Kronmal R, Hart RG. Prevalence, age distribution, and gender of patients with atrial fibrillation. Analysis and implications. *Arch Intern Med* 1995; **155**: 469-73.
- 3) Atrial Fibrillation Investigators: Atrial Fibrillation, Aspirin, Anticoagulation Study; Boston Area Anticoagulation Trial for Atrial Fibrillation Study; Canadian Atrial Fibrillation Anticoagulation Study; Stroke Prevention in Atrial Fibrillation Study; Veterans Affairs Stroke Prevention in Nonrheumatic Atrial Fibrillation Study. Risk factors for stroke and efficacy of anti-thrombotic therapy in atrial fibrillation. Analysis of pooled data from five randomized controlled trials. *Arch Intern Med* 1994; **154**: 1449-57.
- 4) Patients with nonvalvular atrial fibrillation at low risk of stroke during treatment with aspirin: Stroke Prevention in Atrial Fibrillation III Study. The SPAF III Writing Committee for the Stroke Prevention in Atrial Fibrillation Investigators. *Jama* 1998; **279**: 1273-7.
- 5) Kopecky SL, Gersh BJ, McGoon MD, Chu CP, Istrup DM, Chesebro JH, et al. Lone atrial fibrillation in elderly persons: a marker for cardiovascular risk. *Arch Intern Med* 1999; **159**: 1118-22.
- 6) van Latum JC, Koudstaal PJ, Venables GS, van Gijn J, Kappelle LJ, Algra A. Predictors of major vascular events in patients with a transient ischemic attack or minor ischemic stroke and with nonrheumatic atrial fibrillation. European Atrial Fibrillation Trial (EAFT) Study Group. *Stroke* 1995; **26**: 801-6.
- 7) Gage BF, van Walraven C, Pearce L, Hart RG, Koudstaal PJ, Boode BS, et al. Selecting patients with atrial fibrillation for anticoagulation: stroke risk stratification in patients taking aspirin. *Circulation* 2004; **110**: 2287-92.
- 8) Fitzmaurice D. Atrial fibrillation and coagulation: who and when? *Blood Rev* 2009; **23**: 241-4.
- 9) Morgan CL, McEwan P, Tukiendorf A, Robinson PA, Clemens A, Plumb JM. Warfarin treatment in patients with atrial fibrillation: observing outcomes associated with varying levels of INR control. *Thromb Res* 2009; **124**: 37-41.
- 10) Gage BF, Waterman AD, Shannon W, Boechler M, Rich MW, Radford MJ. Validation of clinical classification schemes for predicting stroke: results from the National Registry of Atrial Fibrillation. *Jama* 2001; **285**: 2864-70.
- 11) Masaki N, Suzuki M, Iwatsuka R, Mizukami A, Kumasaka L, Nagahori W, et al. Effectiveness of risk stratification according to CHADS2 score in Japanese patients with nonvalvular atrial fibrillation. *Int Heart J* 2009; **50**: 323-9.
- 12) Crandall MA, Horne BD, Day JD, Anderson JL, Muhlestein JB, Crandall BG, et al. Atrial fibrillation significantly increases total mortality and stroke risk beyond that conveyed by the CHADS2 risk factors. *Pacing Clin Electrophysiol* 2009; **32**: 981-6.
- 13) Acosta S, Bjorck M. Acute thrombo-embolic occlusion of the superior mesenteric artery: a prospective study in a well defined population. *Eur J Vasc Endovasc Surg* 2003; **26**: 179-83.
- 14) Karapolat S, Dag O, Abanoz M, Aslan M. Arterial embolectomy: a retrospective evaluation of 730 cases over 20 years. *Surg Today* 2006; **36**: 416-9.

► Original Article ◀

Preoperative HDL-C Predicts Later Cardiovascular Events after Abdominal Aortic Aneurysm Surgery

Junichiro Takahashi, MD,¹ Yutaka Wakamatsu, MD,¹ Kouji Ishii, MD,¹ Tsuyoshi Kanaoka, MD,¹
Toshihiro Gohda, MD,¹ Shigeyuki Sasaki, MD,² and Yoshiro Matsui, MD³

Purpose: To determine the predictive value of serum lipid levels on the development of later cardiovascular events after abdominal aortic aneurysm (AAA) surgery.

Methods: A total of 101 patients under 70 undergoing an elective AAA surgery were divided into the following two groups: 1) those who developed later cardiovascular events after AAA surgery, including cerebral infarction (n = 4), catheter intervention (PCI) or surgery for coronary artery disease (CAD) (n = 9) and other vascular disease. (CVE group; n = 19); 2) those without later events (NoCVE group; n = 82). Preoperative atherosclerotic risk factors including serum lipid levels were subjected to univariate and multivariate analysis.

Results: The CVE group showed a significantly lower high-density lipoprotein cholesterol (HDL-C) level (32.9 ± 6.6 vs 41.6 ± 12.1 mg/dL; $p < 0.001$), higher low-density lipoprotein cholesterol (LDL-C) / HDL-C ratio (4.30 ± 1.01 vs 3.24 ± 1.15 ; $p = 0.001$), and higher prevalence of mild CAD (without an indication of PCI) ($p = 0.029$) preoperatively. Cox hazard analysis indicated that preexistent mild CAD (hazard ratio 4.70) and preoperative HDL-C < 35 mg/dL (hazard ratio 3.07) were significant predictors for later cardiovascular events after AAA surgery.

Conclusion: Patients at high risk for later cardiovascular events should require a careful follow-up and may also require an aggressive lipid-modifying therapy.

Key words: abdominal aortic aneurysm, dyslipidemia, cardiovascular events

INTRODUCTION

Arteriosclerosis constitutes the principal etiology of abdominal aortic aneurysm (AAA), which is often associated with other arteriosclerotic cardiovascular diseases like coronary artery disease (CAD).^{1–5} Recently,

the importance of appropriate control of dyslipidemia has been emphasized for the primary prevention of atherosclerotic disease.^{6–8} Medications aiming at altering the concentrations of circulating lipids have an established role in occlusive atherosclerosis and recent reports described the role of high-density lipoprotein cholesterol (HDL-C) levels in predicting the risk of AAA development.⁹

Although patients with AAA are at high risk for developing other atherosclerotic cardiovascular disorders, very few reports have described the value of secondary prevention for atherosclerotic disease after AAA surgery, like lipid modifying therapy related to later cardiovascular events.¹⁰ We focused on the atherosclerotic risk factors including serum lipid levels like HDL-C and low-density lipoprotein cholesterol (LDL-C) and investigated the relationship between these risk factors and

¹Division of Cardiovascular Surgery, Aishin Memorial Hospital, Sapporo, Hokkaido, Japan

²Division of Medical Science, Health Sciences University of Hokkaido, Ishikari-Tobetsu, Hokkaido, Japan

³Department of Cardiovascular Surgery, Hokkaido University Graduate School of Medicine, Sapporo, Hokkaido, Japan

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Corresponding author: Shigeyuki Sasaki, MD, PhD. Division of Medical Science, Health Sciences University of Hokkaido, Kanazawa 1757, Ishikari-Tobetsu, Hokkaido 061-0293, Japan
Tel: +81-133-23-1852, Fax: +81-133-23-1852
E-mail: sasakish@hoku-iryo-u.ac.jp

later cardiovascular events after AAA surgery in this study. The purpose was to determine the predictive value of serum lipid levels, as well as other atherosclerotic risk factors, on the development of later cardiovascular events after AAA surgery.

PATIENTS AND METHODS

This retrospective study was performed on 101 patients under 70 who underwent an elective repair of non-ruptured AAA between August 1988 and December 2009 in the Division of Cardiovascular Surgery, Aishin Memorial Hospital. The study subjects were limited to those under the age of 70 at surgery to minimize the influence of aging on the cardiovascular events. All patients were Japanese and consisted of 95 male and 6 female patients with a mean age of 63.2 ± 4.8 years (range from 50 to 69 years). Preexistent atherosclerotic risk factors included a history of treatment of hypertension (HTN) in 66 (65.3 %), diabetes mellitus (DM) in 5 (5%), dyslipidemia treated with statins in 16 (15.8 %), and CAD without an indication for percutaneous catheter intervention (PCI) or coronary artery bypass grafting (CABG) in 32 (31.7 %).

The diagnosis of AAA was established by the findings of enhanced computed tomography (CT) in all cases. In principle patients with AAA greater than 50mm in diameter were determined to have an indication for surgery, and received preoperative coronary artery evaluation by traditional coronary angiography (CAG) or coronary CT (CTCAG). A patient was diagnosed as having CAD when CAG or CTCAG demonstrated that the stenosis was equal to or exceeded 50% ($\geq 50\%$) in at least one major coronary artery or its main branch. The treatment option for the CAD, such as PCI or CABG, was determined by the strategy resembling the Guidelines proposed by American College of Cardiology (ACC) and American Heart Association (AHA) Task Force Report in 1993 and its updated version.^{11, 12)} Patients who had a severe CAD with an indication for PCI or CABG or those with perioperative coronary events were excluded from the study. Patients presenting with CAD without an indication for PCI or CABG were defined as having "mild" CAD in this study. The procedure of AAA repair in this study was a prosthetic aortic replacement with a bifurcated or tube graft in all patients. Patients with mild CAD received perioperative medical treatment with continuous infusion of trinitroglycerin (TNG) at 0.2 to 0.3 $\mu\text{g/kg/min}$ and/or diltiazem (DTZ) at 0.5 to 2.0 $\mu\text{g/kg/min}$. There were no operative deaths and no patients with

inflammatory or infectious aneurysm in this study, and the etiologic source of AAA was considered to be atherosclerosis in all patients.

Follow-up of the patient after discharge has been performed periodically in principle at the outpatient clinic in our institute. Patients who were referred to other hospital or lost to follow-up within 3 months after discharge were not included in this study. Blood pressure at outpatient clinics during the follow-up period was controlled with a target systolic pressure of less than 140 mmHg and diastolic pressure of less than 90 mmHg. Patients with HTN received angiotensin-converting enzyme inhibitors or angiotensin-II receptor blockers concurrently with additional oral calcium-channel blockers as appropriate. The β -blockers were selected in those with CAD unless patients presented with bradycardia, obstructive pulmonary disease, or severe heart failure. There were 79 patients (78%) receiving a treatment of HTN and 10 patients (10%) receiving a treatment of DM postoperatively.

Cardiovascular events during the follow-up period were defined as the occurrence of cerebral infarction, surgery for other vascular disease, the need for PCI or CABG due to CAD, and deaths from unknown causes. According to the cardiovascular events occurrence, the 101 patients investigated in this study were divided into the following two groups: 1) those who developed later cardiovascular events during the follow-up period after AAA surgery (CVE group; $n = 19$); 2) those who developed no events later (NoCVE group; $n = 82$). Clinical features including the age and gender, preexistent risk factors, preoperative and postoperative lipid levels were compared between the two groups. The endpoint of this study for evaluating the rate of freedom from cardiovascular events was defined as the time at cardiovascular events occurrence (CVE group) or time at the end of follow-up for a maximum of 10-years (NoCVE group). The cardiovascular events occurred in the CVE group included the occurrence of cerebral infarction ($n = 4$), the need for PCI or CABG for CAD ($n = 9$), surgery for other vascular diseases ($n = 9$), and death from unknown cause ($n = 1$). In patients with multiple cardiovascular events, the time at the first event was determined as the endpoint of the study. All smokers were requested to stop smoking before AAA surgery.

For the measurement of lipid levels during the study period, blood samples for biochemical examination were in principle collected after an overnight fast, and the serum was separated and analyzed for total cholesterol (TC),

Table 1 Comparative studies of clinical features between the CVE group (n = 19) and the NoCVE group (n = 82)

Clinical Factors	TOTAL (n = 101)	CVE(+) (CVE group; n = 19)	CVE(-) (NoCVE group; n = 82)	p value
Age	63.2 ± 4.8	62.7 ± 4.3	63.4 ± 4.9	0.579
Male/Female	95/6	18/1	77/5	0.89
HTN treatment (%)	66 (65.3 %)	14 (73.7 %)	52 (63.4 %)	0.397
DM treatment (%)	5 (5.0 %)	2 (10.5 %)	3 (3.7 %)	0.214
statins (%)	16 (15.8 %)	5 (26.3 %)	11 (13.4 %)	0.165
CAD (%)	32 (31.7 %)	10 (52.6 %)	22 (26.8 %)	0.029
pre SBP (mmHg)	125.4 ± 18.5	121.8 ± 19.9	126.3 ± 18.2	0.35
pre DBP (mmHg)	70.6 ± 11.7	69.7 ± 14.5	70.8 ± 11.1	0.732
pre HDL-C (mg/dL)	40.0 ± 11.7	32.9 ± 6.6	41.6 ± 12.1	<0.001
pre LDL-C (mg/dL)	127.4 ± 29.1	137.5 ± 25.1	125.2 ± 29.5	0.113
pre LDL-C/HDL-C	3.43 ± 1.19	4.30 ± 1.01	3.24 ± 1.15	0.001
pre TG (mg/dL)	139.1 ± 72.6	140.9 ± 64.6	138.7 ± 74.6	0.906
post HDL-C (mg/dL)	49.4 ± 16.1	49.6 ± 9.5	49.4 ± 17.3	0.934
post LDL-C (mg/dL)	98.3 ± 31.7	92.1 ± 30.6	99.8 ± 32.0	0.34
post LDL-C/HDL-C	2.26 ± 1.28	2.53 ± 1.38	2.18 ± 0.70	0.121
post TG (mg/dL)	102.7 ± 73.9	97.5 ± 42.1	104.0 ± 79.6	0.734
Follow up period (months)	55.2 ± 44.1	48.8 ± 39.5	57.2 ± 46.1	0.466

CVE, cardiovascular events; OR, Odds Ratio; CI, confidence interval; HTN, hypertension; DM, diabetes mellitus; CAD, coronary artery disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglyceride; pre, preoperative; post, postoperative

HDL-C, and triglycerides (TG) using automated assay. Low-density lipoprotein cholesterol (LDL-C) levels were calculated by Friedewald formula. The LDL-C levels during the follow-up period were controlled with a target value of at least less than 130 mg/dL using lipid-modifying medications including statins (n = 49) and fibrates (n = 17) on the physician's preference. The data of postoperative lipid levels of each patient were determined by the optimum value of laboratory data obtained 3 months or later after AAA surgery. The mean follow-up period after discharge until the endpoint of the study was 55.2 ± 44.1 (months). This study was approved by the Hospital Ethics Committee, and all patients received a full explanation of the surgery, related risks, and postoperative treatment strategy by surgeons.

Statistical analysis

Continuous variables are presented as the mean ± standard deviation (SD) and are compared using the Mann-Whitney U-test. The chi-square test was employed for comparisons of nominal variables. The rate of freedom from cardiovascular events (CVE-free rate) was analyzed by the Kaplan-Meier method and comparisons between the two groups were performed by the log-rank

test. The endpoint of each patient for calculating these curves was the day of cardiovascular events occurring in the CVE group and the last follow-up day in the NoCVE group as described above. A Cox proportional hazard model was applied to determine the effects of variables on cardiovascular events during the follow-up period. Differences were statistically considered significant at p < 0.05. SPSS (Ver.12.0J) software (SPSS Inc., Chicago, IL) was used for all statistical analysis.

RESULTS

Overview of the clinical characteristics and atherosclerotic risk factors compared between the CVE and NoCVE group is summarized in the Table 1. In univariate analysis of preoperative factors, there were no significant differences in the age, gender, systolic and diastolic blood pressure, incidence of a history of HTN, DM, and statins treatment between the two groups. The prevalence of mild CAD was significantly higher in the CVE group than in the NoCVE group (odds ratio (OR) 3.03, 95% confidence interval (CI) 1.09 to 8.44; p = 0.029). Regarding preoperative serum lipid levels, patients in the CVE group showed a significantly lower HDL-C level (32.9 ±

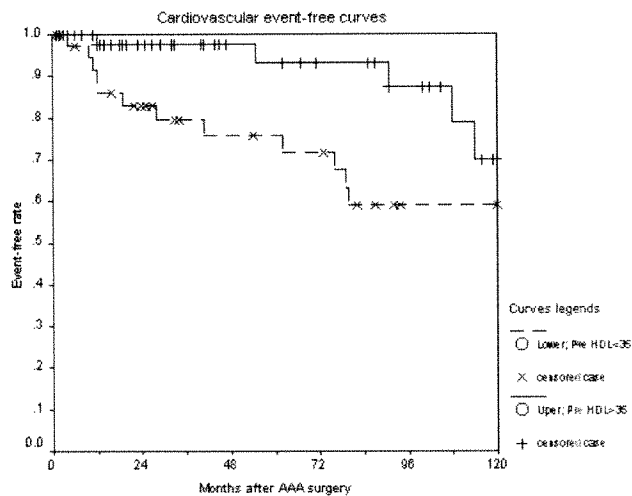


Fig. 1 Kaplan-Meier curves indicating freedom from cardiovascular events in the group of patients with the preoperative HDL-C ≤ 35 and those with HDL-C > 35 (mg/dL).

6.6 vs 41.6 ± 12.1 mg/dL; $p < 0.001$), higher LDL-C/HDL-C ratio (4.30 ± 1.01 vs 3.24 ± 1.15 ; $p = 0.001$) than those of the NoCVE group. Differences of the serum LDL-C levels and triglyceride levels did not reach statistical significance.

Serum lipid levels during the follow-up period after AAA surgery are also shown in the Table 1 as postoperative values. There were no significant differences in the postoperative HDL-C, LDL-C, and TG levels and LDL-C/HDL-C ratio. The mean follow-up period was 48.8 ± 39.5 (range 4 to 114) months for the CVE group and 57.2 ± 46.1 (range 3 to 120) months for the NoCVE group, which showed no significant difference ($p = 0.47$). There were 5 deaths in the NoCVE group during the follow-up period, including deaths from lung cancer ($n = 2$; at 31 and 102 months after surgery), esophageal cancer ($n = 1$; 87 months after surgery), pneumonia ($n = 1$; 91 months after surgery), and head injury ($n = 1$; 6 months after surgery). These cases were represented as censored cases in the calculation of the Kaplan-Meier method and a Cox proportional hazard model. In the CVE group, one patient died from unknown cause as described above.

Since the HDL-C levels were significantly different between the two groups, we compared the cardiovascular event-free (CVE-free) rate between patients with preoperative serum HDL-C levels ≤ 35 mg/dL ($n = 44$) and those with HDL-C levels > 35 mg/dL ($n = 57$). The cut-off value (35 mg/dL) was calculated from receiver-operating characteristics curves (ROC curve) using statistical software. **Figure 1** shows a comparison of Kaplan-Meier

Table 2 Relationship between risk factors and cardiovascular events by multivariate analysis using Cox proportional hazard model

Risk Factors	Hazard Ratio	95% CI	p value
Age	0.97	0.86–1.09	0.561
HTN	1.14	0.33–3.94	0.837
DM	1.84	0.54–6.27	0.329
CAD	4.7	1.70–12.98	0.003
HDL-C ≤ 35	3.07	1.06–8.86	0.038
TG	1	0.99–1.01	0.516

CI, confidence interval; HTN, hypertension; DM, diabetes mellitus; CAD, coronary artery disease; SBP, systolic blood pressure; DBP, diastolic blood pressure; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; TG, triglyceride

curves indicating the rate of freedom from cardiovascular events between the two patient groups divided based on the preoperative HDL-C levels. As shown in the Figure 1, there was a significant difference in the CVE-free rate depending on the preoperative HDL-C levels. Patients with preoperative HDL-C levels > 35 mg/dL had a significantly better CVE-free rate ($p = 0.033$ by the log-rank test).

Based on the results from univariate analysis and CVE-free rate analysis, clinical factors that may be related to the development of cardiovascular events were assessed with multivariate analysis using Cox proportional hazard model with stepwise method to identify correlations with the later events occurrence. The items assessed included an age, a history of treatment of HTN and DM, presence of preexistent mild CAD, the serum HDL-C levels ≤ 35 mg/dL, and TG levels as preoperative factors. The results are shown in the Table 2, which indicated that the cardiovascular event occurrence was significantly correlated with the presence of a mild CAD (hazard ratio 4.70, $p = 0.003$) and the serum HDL-C levels ≤ 35 (mg/dL) (hazard ratio 3.07, $p = 0.038$) in the preoperative factors.

DISCUSSION

AAA is an asymptomatic condition with a high mortality rate related to rupture, which has been the cause of 1% to 2% of all deaths in the Western world.^{1, 13} Several studies reported a coexistence of atherosclerosis or disturbed connective tissue metabolism with AAA as an underlying etiology,^{1, 2, 14} but the evidence for the role of lipids in the development of an AAA remains to be

controversial.¹⁵⁻¹⁷ Hobbs et al reported the highly significant association between LDL-C and small AAA, and LDL-C could be an initiating factor in the development of an AAA.¹⁵ A recent report by Golledge et al. indicated that HDL-C appeared to be the most important lipid in predicting the risk of AAA development.⁹ Forsdahl et al. described the association of statin prescription with the development of an AAA in their report from the Tromso study.¹¹ These reports mainly described the primary prevention of the development of an AAA, but few reports mentioned the secondary prevention for atherosclerotic disease after AAA surgery.¹⁰ As AAA represents a progress in systemic atherosclerosis, patients undergoing surgical treatment of AAA should be followed up to prevent other cardiovascular disorders.

In general, increasing age is consistently identified as a strong risk factor for atherosclerotic disease like AAA in the past literature¹¹; thus, the age distribution of the study group may have a significant influence on the results from the study like this investigation. For example, the Tromso study included a very wide range of ages (25 to 82 years); thus, the results may not reflect the true risk factors because the risk period for the development of an AAA did not occur for many patients aged ≤ 50 years during the study period.¹¹ To minimize the influence of aging on the events during the follow-up period, the subjects in this study were limited to those under 70 (range 50 to 69) at surgery.

In the analyses of preoperative factors, the prevalence of mild CAD, the serum HDL-C levels and LDL-C/HDL-C ratio were found to have significant differences between the CVE group and the NoCVE group. The mean preoperative HDL-C level in all patients was as low as 40.0 ± 11.7 mg/dL, and the LDL-C/HDL-C ratio was as high as 3.43 ± 1.19 , which were consistent with results from previous reports describing that decrease in the HDL-C levels and increase in the LDL-C/HDL-C ratio enhanced the risk for the development of an AAA.^{9, 15} Our results showing that further decrease in the preoperative HDL-C levels enhanced the risk for cardiovascular events after AAA surgery may be reasonable, and there was about a three-fold higher risk of developing cardiovascular events in those with the preoperative HDL-C levels ≤ 35 mg/dL. Patients with preexistent mild CAD are likely to have progression of arteriosclerosis in other arteries; thus, our results seem to be consistent with previous findings.¹⁰

These results indicate that patients at risk for the development of later cardiovascular events, including

those with lowered HDL-C levels < 35 mg/dL and those with preexistent CAD, should be carefully followed-up to prevent later cardiovascular events after AAA surgery. In general, LDL-C at a high serum level may accumulate in the artery wall where they are oxidized and taken up by foam cells in a process that leads to the development and progression of atherosclerosis.⁶ HDL-C is reported to oppose atherosclerosis by removing cholesterol from foam cells, by inhibiting the oxidation of LDLs, and by limiting the inflammatory processes that underlie atherosclerosis.⁶ Based on these findings, some reports advocated that LDL-C/HDL-C ratio can be used as a beneficial treatment index although the serum LDL-C levels are mainly employed as a treatment target in previous reports.^{1, 15, 18} Based on our results, HDL-C may play an important role not only in the development of AAA⁹ but also in the development of later cardiovascular events after AAA surgery. Patients in our series generally had a low level of HDL-C, but those with preoperative HDL-C levels ≤ 35 may have a further higher risk for the development of cardiovascular events after AAA surgery.

There are some limitations in this study. In our study design, patients with AAA were retrospectively divided into the two groups based on the patient outcome as to whether they had cardiovascular events or not later, as a single center experience. Lipid-modifying therapy was not given to all patients after surgery based on the condition of patients. Ideally, a randomized prospective study is required to determine the value of predictor with a larger number of patients. Second, the findings of our study were limited to those aged < 70 at surgery; thus, the value of lipid-modifying therapy in patients with age older than the present study group is unknown. Since the majority of subjects were male patients, we can draw no conclusions on the association of lipids with cardiovascular events in women. Third, the follow-up period is relatively short in some patients; thus, the short follow-up period may influence the incidence of cardiovascular events. Although there are many limitations, our study results may help to understand the predictive value of serum lipid levels and to prognosticate the outcome at least in part of patients with AAA.

In conclusion, our study indicated that a decrease in the preoperative HDL-C levels ≤ 35 mg/dL and the presence of CAD were significant predictors for the development of later cardiovascular events during follow-up after AAA surgery. These patients at high risk for later cardiovascular events should require a careful follow-up and may also require an aggressive lipid-modifying therapy.

REFERENCES

- 1) Forsdahl SH, Singh K, Solberg S, Jacobsen BK. Risk factors for abdominal aortic aneurysms: A 7-year prospective study: The Tromso Study, 1994-2001. *Circulation* 2009; **119**: 2202-8.
- 2) Singh K, Bonna KH, Jacobsen BK, Bjork L, Solberg S. Prevalence of and risk factors for abdominal aortic aneurysms in a population-based study. *Am J Epidemiol* 2001; **154**: 236-44.
- 3) Golledge J, Muller J, Daugherty A, Norman P. Abdominal aortic aneurysm: pathogenesis and implications for management. *Arterioscler Thromb Vasc Biol* 2006; **26**: 2605-13.
- 4) Golden MA, Whittemore AD, Donaldson MC, Mannick JA. Selective evaluation and management of coronary artery disease in patients undergoing repair of abdominal aortic aneurysms. A 16-year experience. *Ann Surg* 1990; **212**: 415-20.
- 5) Takahashi J, Okude J, Gohda T, Murakami T, Hatkeyama M, Sasaki S, et al. Coronary artery bypass surgery in patients with abdominal aortic aneurysm: detection and treatment of concomitant coronary artery disease. *Ann Thorac Cardiovasc Surg* 2002; **8**: 213-9.
- 6) Barter P. The role of HDL-cholesterol in preventing atherosclerotic disease. *Eur Heart J* 2005; **7** (suppl F): F4-F8.
- 7) LaRosa JC, Grundy SM, Waters DD, Shear C, Barter P, Fruchart J-C, et al. Intensive lipid lowering with atorvastatin in patients with stable coronary disease. *N Engl J Med* 2005; **352**: 1425-35.
- 8) Nakamura H, Mizuno K, Group MS. Abstract 6282: Lowered ratio of low-density lipoprotein cholesterol to high-density lipoprotein cholesterol with lipid lowering therapy associated with reduction of cardiovascular events in primary prevention: MEGA study post-hoc analysis. *Circulation* 2008; **118**: S1174.
- 9) Golledge J, Bockxmeer Fv, Jamrozik K, McCann M, Norman PE. Association between serum lipoproteins and abdominal aortic aneurysm. *Am J Cardiol* 2010; **105**: 1480-4.
- 10) Smith SC Jr, Allen J, Blair SN, Bonow RO, Brass LM, Fonarow GC, et al. AHA/ACC Guidelines for secondary prevention for patients with coronary and other atherosclerotic vascular disease: 2006 Update: Endorsed by the National Heart, Lung, and Blood Institute. *J Am Coll Cardiol* 2006; **47**: 2130-9.
- 11) Smith SC Jr, Dove JT, Jacobs AK, Kennedy JW, Kereiakes D, Kern MJ, et al. ACC/AHA guidelines of percutaneous coronary interventions (revision of the 1993 PTCA guidelines)--executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (committee to revise the 1993 guidelines for percutaneous transluminal coronary angioplasty). *J Am Coll Cardiol* 2001; **37**: 2215-39.
- 12) Smith SC Jr, Feldman TE, Hirshfeld JW Jr, Jacobs AK, Kern MJ, King SB 3rd, et al. ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention--Summary Article: A Report of the ACC/AHA Task Force on Practice Guidelines (ACC/AHA/SCAI Writing Committee to Update the 2001 Guidelines for Percutaneous Coronary Intervention). *J Am Coll Cardiol* 2006; **47**: 216-35.
- 13) Wilmink TB, Quick CR, Hubbard CS, Day NE. The influence of screening on the incidence of ruptured abdominal aortic aneurysms. *J Vasc Surg* 1999; **30**: 203-8.
- 14) Wilmink AB, Quick CR, Hubbard CS, Day NE. The association between connective tissue laxity and the risk of an abdominal aortic aneurysm. *Eur J Vasc Endovasc Surg* 2000; **20**: 290-5.
- 15) Hobbs SD, Claridge MW, Quick CR, Day NE, Bradbury AW, Wilmink AB. LDL Cholesterol is associated with small abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg* 2003; **26**: 618-22.
- 16) Wanhainen A, Bergqvist D, Boman K, Nilsson T, Rutegard J, Bjorck M. Risk factors associated with abdominal aortic aneurysm: A population-based study with historical and current data. *J Vasc Surg* 2005; **41**: 390-6.
- 17) Ferguson CD, Clancy P, Bourke B, Walker PJ, Dear A, Buckenham T, et al. Association of statin prescription with small abdominal aortic aneurysm progression. *Am Heart J* 2010; **159**: 307-13.
- 18) Brunzell JD, Davidson M, Furberg CD, Goldberg RB, Howard BV, Stein JH, et al. Lipoprotein management in patients with cardiometabolic risk: Consensus statement from the American Diabetes Association and the American College of Cardiology Foundation. *Diabetes Care* 2008; **31**: 811-22.

➤ Case Report ◀

Fatal Pulmonary Thromboembolism due to Inferior Vena Cava Thrombosis

Boonsak Hanterdsith, MD

Pulmonary embolism (PE) is one of the most undiagnosed causes of death, and more than half of fatal PE is discovered only during autopsy. The author reports a case of sudden death from massive pulmonary thromboembolism due to an inferior vena cava (IVC) thrombosis caused by chronic pancreatitis. An extensive search for the location of the thrombus identified the source of emboli. The probable mechanism of IVC thrombosis caused by chronic pancreatitis is discussed. Awareness of this serious complication of chronic pancreatitis may have prevented the sudden death.

Key words: fatal pulmonary thromboembolism, inferior vena cava thrombosis, chronic pancreatitis

INTRODUCTION

The incidence of pulmonary embolism (PE) varies according to location.^{1,2} In the USA, of fatalities related to venous thromboembolism, 34% were sudden death.² The German pathologist, Rudolf Ludwig Karl Virchow (1821–1902), has described three factors predisposing venous thrombosis i.e. changes in the vessel wall, pattern of blood flow, and blood constituents.³ These predisposing factors are known as the “Virchow’s triad.” More than 95% of all pulmonary emboli arise from thrombi within the large deep veins of the lower legs, typically originating in the popliteal vein and the larger veins above it.¹ Important risk factors include prolonged bed rest, surgery (especially orthopedic surgery of the knee and hip), severe trauma, burns, congestive heart failure, parturition, high-estrogen contraceptive use, disseminated cancer, and primary disorder of hypercoagulability.¹ Chronic pancreatitis, however, is a rare cause of thrombosis in venous vessels.

Division of Forensic Medicine, Lamphun Hospital, Lamphun, Thailand

Received: December 20, 2010; Accepted: January 24, 2011
Corresponding author: Boonsak Hanterdsith, MD. Division of Forensic Medicine, Lamphun Hospital, Lamphun 51000, Thailand
Tel: +66-0-8678-12869, Fax: +66-0-5356-9191
E-mail: trapezius60@yahoo.com

CASE REPORT

On July 22, 2008, a 29-year-old male collapsed at home and was brought to the emergency room of the Lamphun Hospital by his wife. The initial clinical presentations were unconsciousness, breathlessness, absence of pulse, dilated and fixed pupils, and cold cyanotic skin. Attempted resuscitation was unsuccessful, and he was pronounced dead on arrival. According to his wife, he woke up at about 2 a.m. with palpitations and then fell to the floor. He had no serious medical history or family history of Sudden Unexplained Death Syndrome (SUDS). He drank alcohol occasionally, and his smoking status was unknown. His father committed suicide by a gunshot to the head. His mother has no serious illness. His grandmother and some relatives have diabetes mellitus. The first visit to Lamphun Hospital was on October 23, 2005 because of subepigastric pain and vomiting. The symptoms began at about midnight after drinking alcohol all night. His blood pressure was 120/60 mmHg with a regular pulse rate at 80 beats/min. He weighed 75 kg. The doctor diagnosed gastritis and scheduled a follow-up visit; however, the patient did not return for treatment. On September 13, 2006 (approximately 11 months later) he came to the out-patient department (OPD) with left-sided abdominal and subepigastric pain, and abdominal bloating. He reported that he has occasional stomach-aches and takes medicine to relieve the symptoms. His blood pressure was 110/60 mmHg and the body tempera-

Table 1 Laboratory results of the deceased in 2006

Laboratory results		Normal value	Laboratory results		Normal value
serum amylase (U/L)	337	29–103	AST [†] (U/L)	55	10–37
BUN [‡] (mg/dL)	12	8–20	ALT [‡] (U/L)	47	10–45
serum creatinine (mg/dL)	1.0	0.8–1.4	alkaline phosphatase (U/L)	109	34–104
serum sodium (mmol/L)	127	135–145	serum magnesium (mg/dL)	2.3	1.8–2.6
serum potassium (mmol/L)	4.4	3.4–5.1	hemoglobin (g/dL)	18.0	13–17
serum chloride (mmol/L)	92	98–106	hematocrit (%)	53.5	38–50
serum CO ₂ (mmol/L)	24	21–41	WBC [§] (cells/ml)	13330	5000–10000
serum total protein (mg/dL)	6.9	6.6–8.3	neutrophil (%)	92.5	45–79
serum albumin (g/dL)	3.9	3.5–5.2	lymphocyte (%)	4.2	20–45
serum globulin (g/dL)	3.0	2.4–3.2	platelet count (cells/ml)	184000	150000–400000
total bilirubin (mg/dL)	1.5	0.3–1.2	non-fasting blood glucose (mg/dL)	150	74–146
direct bilirubin (mg/dL)	0.3	0.0–0.2			

[†] Aspartate aminotransferase; [‡] Blood urea nitrogen; [§] Alanine aminotransferase; [§] White blood count

ture was normal. He was admitted to the hospital for further investigation (**Table 1**).

The clinical and laboratory results indicated acute pancreatitis. He was treated until he was free of symptoms, and after 5 days, he was discharged from the hospital. On May 28, 2008 (approximately 1.5 year later), he came to the OPD with symptoms similar to his previous visit: left-sided abdominal pain and all-night flatulence. The doctor diagnosed dyspepsia and treated him with 50 mg of ranitidine via intravenous injection, 150 mg of ranitidine (oral) twice a day, domperidone (oral) three times a day, and 500 mg of paracetamol (oral).

The autopsy was performed ten hours after death. The deceased was normal height (174 cm) and weight. There were recent multiple subcutaneous contusions, 2–8 cm, on the medial aspect of both arms, posterior aspect of the left arm, and anterior aspect of the right forearm. The conjunctivae showed no petechial hemorrhage. No injection mark or fatal wound was observed on the body.

The internal examination revealed no injury of vital organs. The thyroid gland was of normal size and shape. No foreign body obstructed the airway passage. Both lungs showed pulmonary edema without mass lesion. There was a sausage-like thrombus, 6 cm in length and 2 cm in diameter, obstructing the left main pulmonary artery. The thrombus was dull with a striated surface, and had a firm consistency which is consistent with a

premortem blood clot. Many streaks of thrombi occupied the small distal pulmonary arteries. The right lung and the left lung weighed 480 gm and 500 gm, respectively. The heart weighed 300 gm and had a normal shape. All major coronary arteries were widely patent. There were wide-spread areas of flame-shaped hemorrhage in the subendocardial left ventricular free wall and the inter-ventricular septum (IVS). The left ventricular free wall and IVS were equally thick. No valvular or congenital abnormality was observed. There was no thrombus in the heart chambers. The internal organs of the abdomen showed no gross injury. The liver, small bowel, large bowel, both kidneys, and both adrenal glands had normal weight without significant gross pathologic abnormality. The spleen weighed 240 gm without an infiltrative mass lesion (diffuse enlargement). The pancreas had a firm consistency due to fibrosis and adhered firmly to the adjacent organs. There was no intrapancreatic duct or biliary tract stone. The pelvic organs showed no significant gross lesion. The source of the thromboembolism was searched for in the calves, popliteals, thighs, inguinal area, pelvic (iliac veins), IVC, veins of both arms (including veins beneath subcutaneous contusions), and dural venous sinuses. Only the IVC adjacent to the pancreas had a thrombus.

Heart, lung, pancreatic tissue, thrombi in the pulmonary arteries, and the thrombus attached to the IVC were microscopically examined. The myocardial fibers were not enlarged. There was no inflammatory cell infiltrated in the myocardium. There was a coagulative necrosis with some hemorrhage of the right lower lung and left lower lung tissues. All sections of thrombi were consistent with a pre-mortem clot. The tissue between the pancreas and adjacent IVC had some fibroses. The tissue of pancreas especially adjacent to IVC thrombosis had fibroses and was surrounded by lymphocytes. The acini of the pancreatic tissue were decreased. No malignancy cells were detected.

DISCUSSION

Pulmonary thromboembolism, secondary to pancreatitis, and IVC thrombosis do occur,^{4–7)} though a fatal outcome is rare. Pulmonary embolism is the most undiagnosed cause of death clinically. More than half of fatal PE were diagnosed only during autopsy.^{8, 9)} More than three-quarters of the victims had predisposing factors, but the remaining 20% of pulmonary embolism deaths have not been identified predisposing factor.⁸⁾ In this

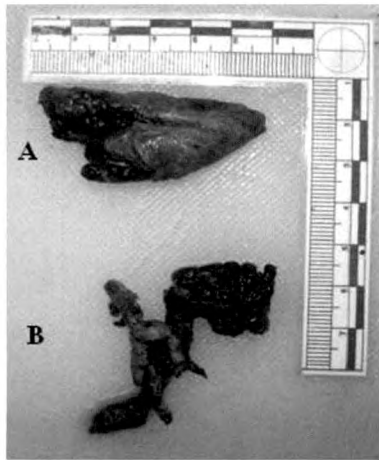


Fig. 1 Gross examination of the thrombus in the pulmonary artery. (A) Large premortem thrombus recovered from the left main pulmonary artery. The proximal part is on the right side. (B) Many streaks of premortem thrombi, recovered from distal pulmonary arteries.

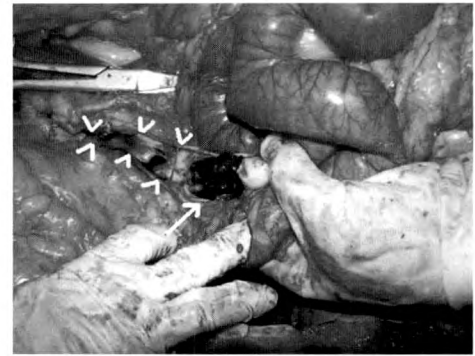


Fig. 2 IVC was explored longitudinally (arrow head) to show the premortem thrombus (arrow).

case, all major venous vessels were explored to search for the source of the thromboemboli. The deep veins of both arms were explored because of overlying skin contusion, but there was no thrombosis. Only the IVC adjacent to the pancreas showed thrombosis that was correlated with pancreatitis. The suggested mechanism of thrombosis caused by pancreatitis is trypsin converts prekallikrein to its activated form, thus sparking the kinin system and, by activation of factor XII, also sets the complement system and clotting in motion.¹⁾ However, predisposing factors of thrombosis in this case may be more than one cause. Another potential cause of venous thrombosis in this case might be a hereditary coagulation disorder, as this was not assessed prior to the patients' death. Apparently, venous thrombotic complications of pancreatitis are common, but mainly affect the splenic vein, portal vein or superior mesenteric vein.¹⁰⁻¹²⁾ One study reported recurrent pancreatitis in pregnancy that lead to IVC thrombosis; however, it was not complicated by pulmonary thromboembolism.¹³⁾ The probable mechanism of splenomegaly may be from high venous pressure in the portal system caused by IVC thrombosis. Awareness of this serious complication of chronic pancreatitis may have prevented sudden death in this case. The doctor should have investigated further to obtain a correct diagnosis other than dyspepsia using gastrointestinal endoscopy or imaging (ultrasonography or CT scanning) which might have visualized early forming thrombus in the IVC. On the other hand, if the patient were concerned about his symptoms, he should have returned for his regular, follow-up visits. In case of recurrent pancreatitis which previously caused IVC thrombosis may have benefit to prevent recurrent IVC thrombosis by thrombolytic prophylaxis.¹³⁾

REFERENCES

- 1) Kumar V, KA Abul, F Nelson, NM Richard, editors. Robbins basic pathology. 8th ed. Philadelphia: Saunders Elsevier, 2007: 504-5678.
- 2) Samuel Z. Goldhaber SZ. Deep venous thrombosis and pulmonary thromboembolism. In: Kasper DL, Braunwald E, Fauci AS, Hauser SL, Longo DL, Jameson JL, Loscalzo J, editors. Harrison's principles of internal medicine. 17th ed. USA: McGraw-Hill, 2008: 1651-7.
- 3) Dickson BC. Venous thrombosis: on the history of Virchow's triad. UTMJ 2004; **81**: 166-71.
- 4) Stringer MD, Michell M, McIrvine AJ. Inferior vena caval thrombosis complicating acute pancreatitis. Case report. Acta Chir Scand 1988; **154**: 161-3.
- 5) Antony SJ, Loomis T, Brumble L, Hannis MD. Inferior vena caval thrombosis associated with acute pancreatitis: an unusual vascular complication--its presentation and management. Angiology 1994; **45**: 1009-14.
- 6) Ma SK, Kim SW, Kim NH, Choi KC. Renal vein and inferior vena cava thrombosis associated with acute pancreatitis. Nephron 2002; **92**: 475-7.
- 7) Ohta H, Hachiya T. A case of inferior vena cava thrombosis and pulmonary embolism secondary to acute exacerbation of chronic pancreatitis: a rare finding in radionuclide venography. Ann Nucl Med 2002; **16**: 147-9.
- 8) Saukko P, Knight B. Knight's forensic pathology. 3rd ed. London: Arnold, 2004: 340, 513.
- 9) Stevanovic G, Tucakovic G, Dotlic R, Kanjuh V. Correlation of clinical diagnoses with autopsy findings: A retrospective study of 2,145 consecutive autopsies. Hum Pathol 1986; **17**: 1225-30.
- 10) Dörffel T, Wruck T, Rückert RI, Romaniuk P, Dörffel Q, Wermke W. Vascular complications in acute pancreatitis assessed by color duplex ultrasonography. Pancreas 2000; **21**: 126-33.
- 11) Vujic I. Vascular complications of pancreatitis. Radiol Clin North Am 1989; **27**: 81-91.
- 12) Warshaw AL, Jin GL, Ottinger LW. Recognition and clinical implications of mesenteric and portal vein obstruction in chronic pancreatitis. Arch Surg 1987; **122**: 410-15.
- 13) Inferior vena cava thrombosis and recurrent pancreatitis in pregnancy. J Obstet Gynaecol 2006; **26**: 372-3.

» **Case Report** «

Delayed Postoperative Paraplegia and Graft Infection after a Thoracoabdominal Dissection

Kengo Nishimura, MD, PhD,¹ Azumi Matsumura, MD,¹ Shigeto Miyasaka, MD, PhD,¹
Hiroyuki Maeta, MD, PhD,¹ Keisuke Morimoto, MD, PhD,¹ and Iwao Taniguchi, MD, PhD²

We report the successful treatment of thoracoabdominal dissection, which extended into the left iliac artery, despite two independent complications: graft infection and a relatively rare, delayed postoperative paraplegia. The paraplegia suddenly occurred on postoperative day 10, and after an intravenous infusion of heparin and methylprednisolone, it gradually subsided. Moreover, graft infection was diagnosed on postoperative day 27, and with continuous irrigation of antibiotic treatment it was cured without recurrence of infection. Although anticoagulation therapy is not indicated for paraplegia, we suppose that it might be used as an adjunct therapeutic.

Key words: delayed postoperative paraplegia, graft infection, thoracoabdominal dissection

INTRODUCTION

Spinal cord injury is the most critical complication in the treatment of descending thoracic and thoracoabdominal aneurysms, either involving open surgical repair or endovascular techniques.^{1–3)} In contrast to immediate spinal cord deficits, delayed neurologic injury has attracted little attention and remains poorly understood.⁴⁾ Graft infection is a life-threatening and treatment-resistant complication, especially after thoracoabdominal aneurysm repair. We report successful treatment of thoracoabdominal dissection, which extended into left iliac artery, despite two independent complications of relatively rare, delayed postoperative paraplegia and graft infection.

¹Department of Thoracic and Cardiovascular Surgery, Tottori Prefectural Central Hospital, Tottori, Tottori, Japan

²Department of Cardiovascular Surgery, Tottori Red Cross Hospital, Tottori, Tottori, Japan

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Corresponding author: Kengo Nishimura, MD, PhD. Department of Thoracic and Cardiovascular Surgery, Tottori Prefectural Central Hospital, 730 Ezu, Tottori 680-0901, Japan
Tel: +81-857-26-2271, Fax: +81-857-29-3227
E-mail: nishimurakengo@hotmail.com

CASE

A 54-year-old man with a history of hypertension had sudden-onset back pain in May 2009 and was referred to the Tottori Red Cross Hospital, Tottori, Japan. The patient was prescribed antihypertensive medication and was discharged; however, one month later, he returned to the hospital with another episode of sudden-onset back pain. Enhanced chest and abdominal computed tomography (CT) on the initial admission revealed thoracoabdominal dissection, which extended into the left common iliac artery (CIA) measuring 55 × 68 mm in maximum diameter. Physical examination was unremarkable except for being overweight (height, 172 cm; weight, 90 kg). The results of blood examination, electrocardiogram, and echocardiography were normal. The CT on the second admission revealed another dissection and expansion of the aneurysm measuring 61 × 71 mm in diameter (**Fig. 1**). All abdominal branches originated from the true lumen. After the dissection and expansion of the aneurysm, we decided to operate by employing a four-branched graft for the proximal part and a bifurcated graft for the distal part. During surgery, we drained the cerebrospinal fluid (CSF) and monitored transcranial motor evoked potentials (MEP). We repositioned the patient in the right lateral decubitus position and made the incision at the sev-

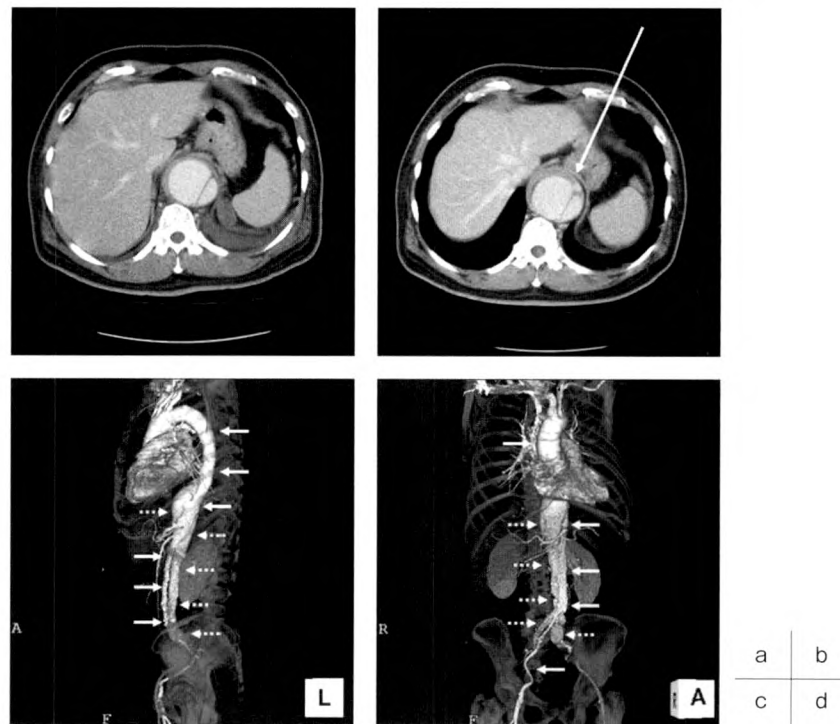


Fig. 1 Preoperative enhanced CT.

a) Enhanced CT on the first admission reveals a dissecting thoracoabdominal aortic aneurysm measuring 55×68 mm in maximum diameter. b) Enhanced CT on the second admission shows another dissection and expansion of the aneurysm, measuring 61×71 mm in diameter. c) Lateral view of three-dimensional CT (3DCT) showing a true (solid arrow) and false (dotted arrow) lumen. d) Right anterior oblique view of 3DCT showing a true (solid arrow) and false (dotted arrow) lumen.

CT, computed tomography

enth intercostal space to the costal cartilage, proceeded to cut obliquely to the umbilicus and then to above the symphysis pubis. A retroperitoneal approach exposed the aorta. After the distal sites of the bilateral external iliac arteries were anastomosed to the bifurcated grafts, we established a percutaneous cardiopulmonary system (PCPS) by inserting a cannula into the arterial branch of the bifurcated graft and then through the left renal vein to the right atrium. We anastomosed the two grafts, celiac trunk, superior mesenteric artery (SMA), two left renal arteries (RAs), right RA, the proximal sites of the descending aorta at the level of Th8, and inferior mesenteric artery (IMA) by sequential segmental repair under normothermic partial cardiopulmonary bypass without cardiac arrest. We also attempted the reattachment of the intercostal arteries, but the aortic wall was too fragile to reconstruct the intercostal arteries. During the operation,

the CSF and MEP were normal. The clamp time of the CA, SMA, one left RA, another RA, a right RA, and the descending aorta was 22, 16, 18, 16, 73, and 81 min, respectively. The total PCPS time was 394 min. The lowest temperature during cardiopulmonary bypass was 34.7°C .

The postoperative CT before the onset of delayed paraplegia showed the occlusion of the right RA and IMA, as well as occlusion of intercostal arteries (**Fig. 2**). On postoperative day 2, we removed the CSF drain, and the patient received intravenous infusion of heparin (15000 units/day) and 1500 mg of methylprednisolone for three days, followed by the administration of warfarin (3 mg/day) and ticlopidine (200 mg/day). On day 10, motor and sensory functions of the lower extremities were impaired, but fortunately, the paraplegia gradually recovered within 6 hours. Moreover, on day 27, the

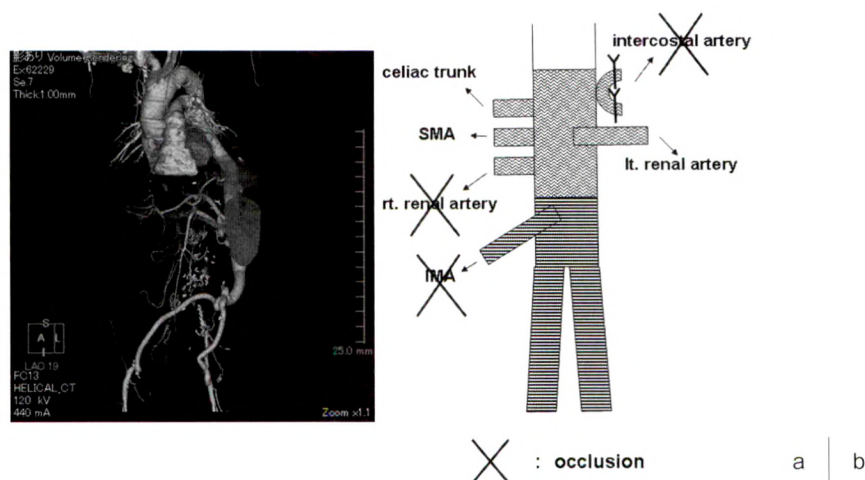


Fig. 2

- a) Postoperative CT scan before the onset of delayed paraplegia.
Scan shows occlusion of the right renal artery and IMA as well as intercostal arteries, patency of celiac trunk, SMA and left renal artery.
- b) The illustration of the postoperative CT.
CT, computed tomography; IMA, inferior mesenteric artery; SMA, superior mesenteric artery

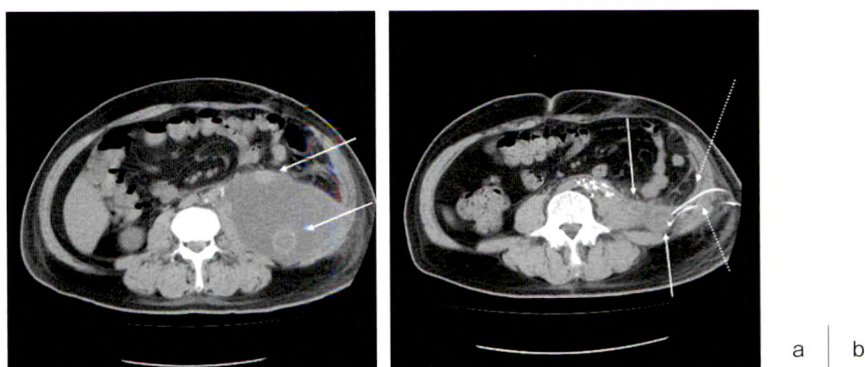


Fig. 3

- a) Postoperative CT scan of postoperative day 27 of two grafts (solid arrow) in the massive fluid accumulation in the left retroperitoneal space.
- b) CT scan of resolved fluid accumulation in the left retroperitoneal space after two drainage tubes (dotted arrow) were placed for the closed irrigation.
CT, computed tomography

patient developed a fever and the abdomen was somewhat distended. The CT showed massive fluid accumulation in the left retroperitoneal space (Fig. 3a). Thus, we placed two drainage tubes into the space with continuous irrigation (saline solution of 250 ml/hour) for 14 days and intermittent irrigation (saline solution of 1000 ml / 4 hours, twice a day) for 5 days (Fig. 3b). Since the space was infected with *Klebsiella oxytoca* (KSBL), sulbactam/

cefoperazone (SBT/ CPZ, 2 g/day for 6 days) and cefmetazole (CMZ, 1 g/day for 2 weeks) were administered intravenously. Closure of the wound was achieved without any residual sign of infection, and the patient was discharged on the postoperative day 60. Later, as a preventative measure, the wound was irrigated daily with minocycline (MINO, 200 mg/day for 1 year).

DISCUSSION

Spinal cord injury is the most critical complication in the treatment of descending thoracic and thoracoabdominal aneurysms that either involve open surgical repair or endovascular strategies.¹⁻³ In contrast to immediate spinal cord deficits, delayed neurologic injury has attracted little attention in the literature and remains poorly understood.⁴ Wong et al.⁵ in their review, reported that the rates of immediate and delayed paraplegia after major TAA repair are 1.7–8.1 and 0.8%–8.1%, respectively. They also described the therapies used to treat delayed paraplegia or paraparesis after thoracoabdominal aortic aneurysm repair in 34 patients: corticosteroids (82%), osmotic diuresis (76%), vasopressor agents (21%), and red blood cell transfusion and intravenous naloxone (6%), as well as CSF drainage (continuation with an existing drain) (9%), drain reinsertion (29%), and the insertion of a new drain (29%).⁵ Safi HJ and colleagues⁶ reported that they keep the mean arterial pressure greater than 90 to 100 mmHg, hemoglobin greater than 10 mg/dL, and cardiac index greater than 2.0 L/min to optimize postoperative spinal cord perfusion and oxygen delivery. As we retrospectively found that the blood pressure (systolic pressure: 100–110 mmHg) was lower than normal from postoperative day 5 after taking antihypertensive medication, the present case may be consistent with the previous reports that delayed paraplegia probably results from a state of malperfusion and postoperative hypotension, leading to spinal cord malperfusion.^{7,8} However, when we consider why it took until postoperative day 5 for the paraplegia to occur, we agree with the report that hypotension is associated with some, but not all, delayed-onset deficits, and other factors may have been important, including rheologic and thrombotic factors.⁹ Moreover, the perfusion of the spinal cord depends on the stabilization of the collateral network of remaining segmental arteries (SAs) after the serial surgical sacrifice of SAs during aneurysm resection.⁷ In the present case, as we can immediately get methylprednisolone and heparin even on the bed side, we chose 1500 mg of methylprednisolone and the intravenous perfusion of heparin (15000 units/day), along with the administration of warfarin (3 mg/day) and ticlopidine (200 mg/day) to keep a rich collateral network. Although the exact mechanism of delayed paraplegia is unknown and anticoagulation therapy is not popular for the paraplegia, we speculate that anticoagulation therapy may be one of the adjunctive therapeutic strategies to maintain a

rich collateral network.

Graft infection is a life-threatening and treatment-resistant complication, especially after thoracoabdominal aneurysm repair. However, in some cases, resection and re-replacement of the infected graft is almost impossible.⁹ Wound irrigation techniques are classified into closed and open irrigation.¹⁰ In the present case, we resolved the infection with appropriate antibiotics by a closed irrigation.

REFERENCES

- 1) Griep RB, Griep EB. Spinal cord perfusion and protection during descending thoracic and thoracoabdominal aortic surgery: the collateral network concept. *Ann Thorac Surg* 2007; **83**: S865–9.
- 2) Conrad MF, Crawford RS, Davison JK, Cambria RP. Thoracoabdominal aneurysm repair: a 20-year perspective. *Ann Thorac Surg* 2007; **83**: S856–61.
- 3) Roselli EE, Greenberg RK, Pfaff K, Francis C, Svensson LG, Lytle BW. Endovascular treatment of thoracoabdominal aortic aneurysms. *J Thorac Cardiovasc Surg* 2007; **133**: 1474–82.
- 4) LeMaire SA, Miller CC 3rd, Conklin LD, Schmittling ZC, Coselli JS. Estimating group mortality and paraplegia rates after thoracoabdominal aortic aneurysm repair. *Ann Thorac Surg* 2003; **75**: 508–13.
- 5) Wong DR, Coselli JS, Amerman K, Bozinovski J, Carter SA, Vaughn WK, et al. Delayed spinal cord deficits after thoracoabdominal aortic aneurysm repair. *Ann Thorac Surg* 2007; **83**: 1345–55.
- 6) Safi HJ, Huynh TT, Estrera AL, Miller CC III. Thoracoabdominal Aortic Aneurysm. In: Rutherford RB. *Vascular Surgery*, sixth edition, Philadelphia: Elsevier Inc, 2005: 1490–511.
- 7) Etz CD, Luehr M, Kari FA, Bodian CA, Smego D, Plestis KA, et al. Paraplegia after extensive thoracic and thoracoabdominal aortic aneurysm repair: does critical spinal cord ischemia occur postoperatively? *J Thorac Cardiovasc Surg* 2008; **135**: 324–30.
- 8) Azizzadeh A, Huynh TT, Miller CC 3rd, Estrera AL, Porat EE, Sheinbaum R, et al. Postoperative risk factors for delayed neurologic deficit after thoracic and thoracoabdominal aortic aneurysm repair: a case-control study. *J Vasc Surg* 2003; **37**: 750–4.
- 9) Ninomiya M, Taketani T, Kubota H, Ohtsuka T, Takamoto S. Open retroperitoneal irrigation for graft infection after thoracoabdominal aortic aneurysm repair. *Jpn J Thorac Cardiovasc Surg* 2003; **51**: 37–40.
- 10) Acinapura AJ, Godfrey N, Romita M, Cunningham J Jr, Adams PX, Jacobowitz JJ, et al. Surgical management of infected median sternotomy: closed irrigation vs. muscle flaps. *J Cardiovasc Surg (Torino)* 1985; **26**: 443–6.

» Case Report «

Retrievable Inferior Vena Cava Filter and Catheter Directed Thrombolysis (CDT) for Treating a 19-year-old Man with Acute Myeloid Leukemia Complicated by Deep Vein Thrombosis (DVT): A Case Report

Hiromi Muranishi, Ryosuke Zushi, Hiroki Nagata, Koji Hasegawa, Atsushi Nakagawa, and Hidefumi Hamada

Here, we report a case of a 19-year-old man with acute myeloid leukemia complicated by deep vein thrombosis (DVT) in which we placed a retrievable inferior vena cava (IVC) filter during catheter directed thrombolysis (CDT). We were able to retrieve the IVC filter after a successful CDT and concluded that the use of this filter might be efficacious and better than an indwelling IVC filter that is associated with long-term risks. A retrievable filter and CDT should be considered in patients who are at transient risk for phlebotrombosis and require placement of a filter.

Key words: catheter directed thrombolysis, retrievable inferior vena cava filter, deep vein thrombosis

INTRODUCTION

Deep vein thrombosis (DVT) and fatal pulmonary thromboembolism (PTE) can severely worsen the prognosis of the patient. Several researchers have reported that permanent, retrievable inferior vena cava (IVC) filters significantly reduce the development of pulmonary emboli and have been effective in preventing PTE.¹⁾ But, on the other hand, long-term risks have been reported, including migration of the filter, filter occlusion, extensive IVC thrombosis, aortic and vertebral penetration and infection.^{2, 3)} It is also an undeniable fact that patients treated with chemotherapies or those who have undergone bone marrow stem cell transplantation have an increased susceptibility to infection.

We present a case of a young patient with acute myeloid leukemia (AML) who was undergoing chemothera-

pies complicated by DVT, and who we thought might benefit from the use of a retrievable IVC filter and catheter directed thrombolysis (CDT) with urokinase (UK) as the anticoagulant.

CASE REPORT

A 19-year-old man reported that he had had pain and swelling in his right leg, several weeks after the first cycle of several consolidation chemotherapies and treatment involving bone stem cell transplantation, when he was an inpatient in the Department of Hematology, Nissay Hospital, Japan. Contrast-enhanced computed tomography scanning showed thrombotic occlusion from his right iliac vein to femoral vein and no evidence of pulmonary embolism (PE) or extrinsic iliac vein compression (**Fig. 1**). Consequently, he was referred to the department of cardiology for an IVC filter insertion and CDT (Day 1 of intervention).

On physical examination, his height was 167 cm, and weight, 54 kg. Lung and heart sounds were normal. There was swelling and tenderness in his right leg and Homan's sign was positive. On admission, he reported a history of motor paresis in his right leg due to extramedullary tumor; however on day 1, his symptoms seem to

Cardiovascular Internal Medicine, Nissay Hospital, Osaka, Osaka, Japan

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Corresponding author: Hiromi Muranishi, Cardiovascular Internal Medicine, Nissay Hospital, 6-3-8 Itachibori, Nishi-ku, Osaka, Osaka 550-0012, Japan
Tel: +81-6-6543-3581, Fax: +81-6-6543-3581
E-mail: hiromimin3089@hotmail.co.jp

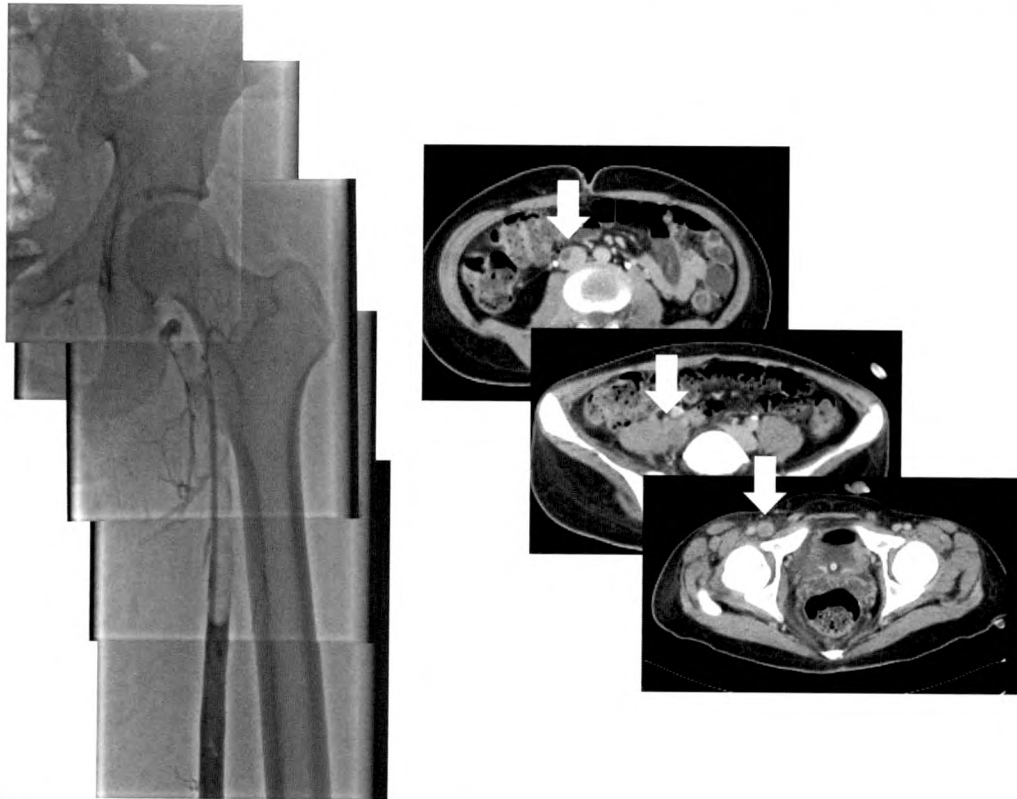


Fig. 1 After insertion of a retrievable IVC filter, we performed an angiography through 4 Fr sheath of his right popliteal vein. This is an angiographic findings in the prone position. The angiography showed thrombotic occlusion from his right iliac artery to SFA. Contrast-enhanced computed tomography scanning showed similar findings.
IVC, inferior vena cava; SFA, superficial femoral artery

have improved, and the chemotherapy had shrunk the tumor. He could move his legs but could not walk without assistance. A blood count revealed hematological complete remission and anemia (white blood cells, $8.32 \times 10^3 / \mu\text{l}$ (neutrophils 70.8%, lymphocytes 14.2%, monocytes 14.4%); hemoglobin, 9.1 g/dl; platelets, $53.9 \times 10^4 / \mu\text{l}$). Chemistry values were normal except for elevations in liver and biliary tract enzymes (alanine aminotransferase (ALT), 45 IU/l; alkaline phosphatase (ALP), 347 IU/l; gamma guanosine triphosphate (γGTP), 62 IU/l; C-reactive protein, 3.18 mg/dl; plasma D-dimer, 8.4 $\mu\text{g}/\text{ml}$; and fibrin degradation product (FDP), 10.4 $\mu\text{g}/\text{ml}$ (normal range for latex agglutination, $<1.0 \mu\text{g}/\text{ml}$ and $<5.0 \mu\text{g}/\text{ml}$). Coagulation studies showed normal levels of protein S antigen, protein C activation and antithrombin III. Lupus anticoagulant was also negative. The echocardiogram showed no significant abnormal findings and lung-perfusion scanning showed no PTE. Venous ultrasoundgraphy showed subtotal thrombotic occlusion from

the right iliac vein to femoral vein and partially organized intramural thrombus in the femoral vein. Magnetic resonance imaging showed a smaller extramedullary tumor compared with findings on admission.

On day 1, we inserted the optional, retrievable IVC filter (LIFE SAVER®, ALN, Bormes-les-Mimosas, France) below the renal vein through the right jugular vein to prevent fatal pulmonary embolism. After that, we placed 4 Fr sheath into the right popliteal vein by an ultrasonical-guided approach and performed an angiography. The angiography showed similar findings to contrast-enhanced computed tomography scanning and venous ultrasoundgraphy (**Fig. 1**). We passed a 0.035-inch straight wire through the thrombotic occluded vein and tried to remove the thrombi by 4 Fr Multipurpose (MP) catheter; however, only a small amount of thrombi was removed, and twenty centimeters-long pulse infusion catheter (Mistique®, Merit Medical Systems Inc., Utah, USA) was placed from iliac vein to femoral vein, but all

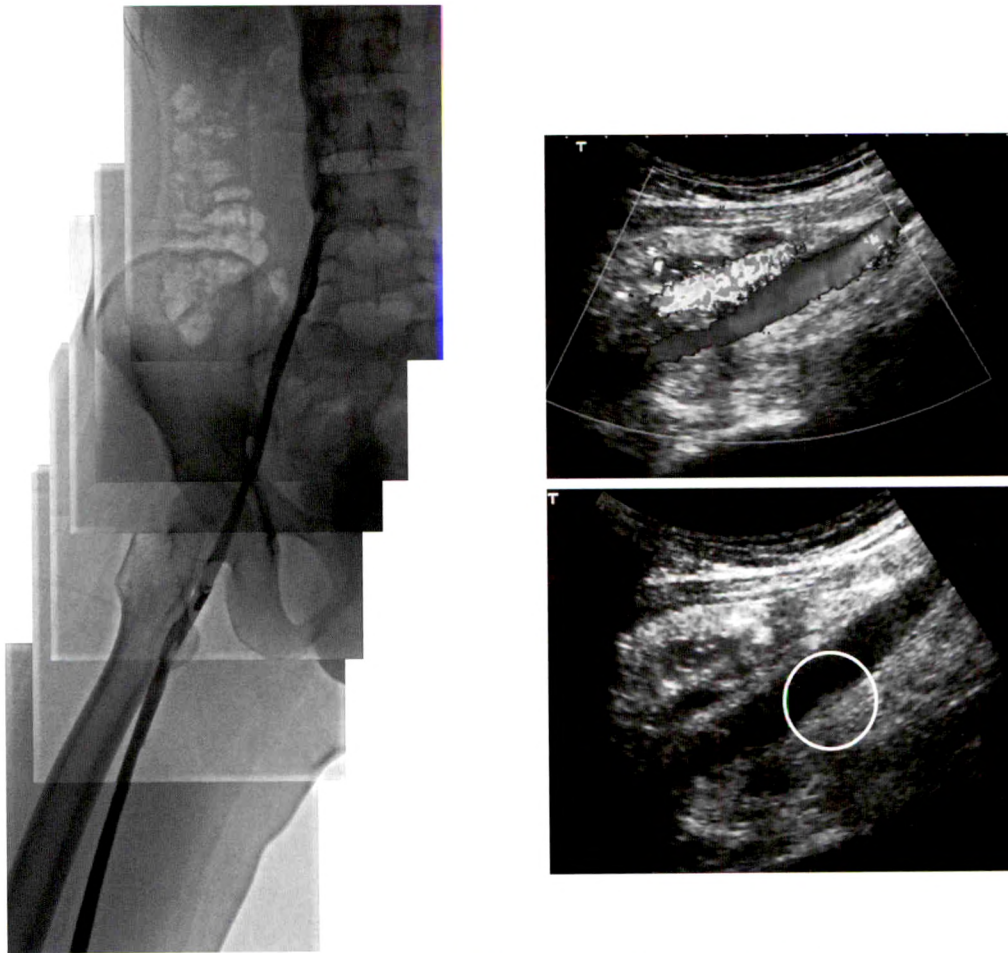


Fig. 2 On day 11, we performed follow up venography and venous ultrasonography. This is an angiographic finding in the spine position. Follow-up venography was performed through the popliteal sheath. It showed a successful thrombolysis; however, the organized intramural thrombus in the femoral vein remained. Venous ultrasonography showed similar findings.

parts of the thrombotic, occluded vein couldn't be covered by the catheter. We began a continuous intravenous administration of heparin to keep the activated partial thromboplastin time (APTT) 1.5–2.0-fold longer than the control value. In addition, 240000 international units (IU) of urokinase (UK) for each time was splashed out of the pulse infusion catheter twice daily for 3 days. On day 4, we replaced the 4 Fr sheath with the 6 Fr sheath, and the follow-up venography showed that the occluded iliac vein remained occluded, with some remaining thrombolysis of the femoral vein and development of collateral vessels. We tried to remove the thrombi again with a larger MP catheter (6 Fr MP catheter), but only some thrombi were removed. Placement of a 20-centimeter-long pulse infusion catheter in all obstructed parts from iliac vein to femoral vein was considered to be better, but we had no

choice but to use a 10-centimeter-long pulse infusion catheter for the occluded iliac vein because the 20-centimeter-long pulse infusion catheter was not available in our hospital at that time and administration of 240000 IU UK each time through the pulse infusion catheter had been continued three times a day. Follow-up venography on day 7 showed more thrombolysis of iliac to femoral vein, but subtotal occlusion due to thrombi remained in several parts of iliac to femoral vein. In a third session, a 20-centimeter-long pulse infusion catheter was placed, and almost all parts of the incomplete thrombotic occluded lesion could be covered. 240000 IU of UK per dose, three times a day was continued for 4 days, and follow-up venography and venous ultrasoundgraphy on day 11 showed disappearance of almost all thrombi except for some organized intramural thrombus left in the femoral vein (**Fig. 2**).

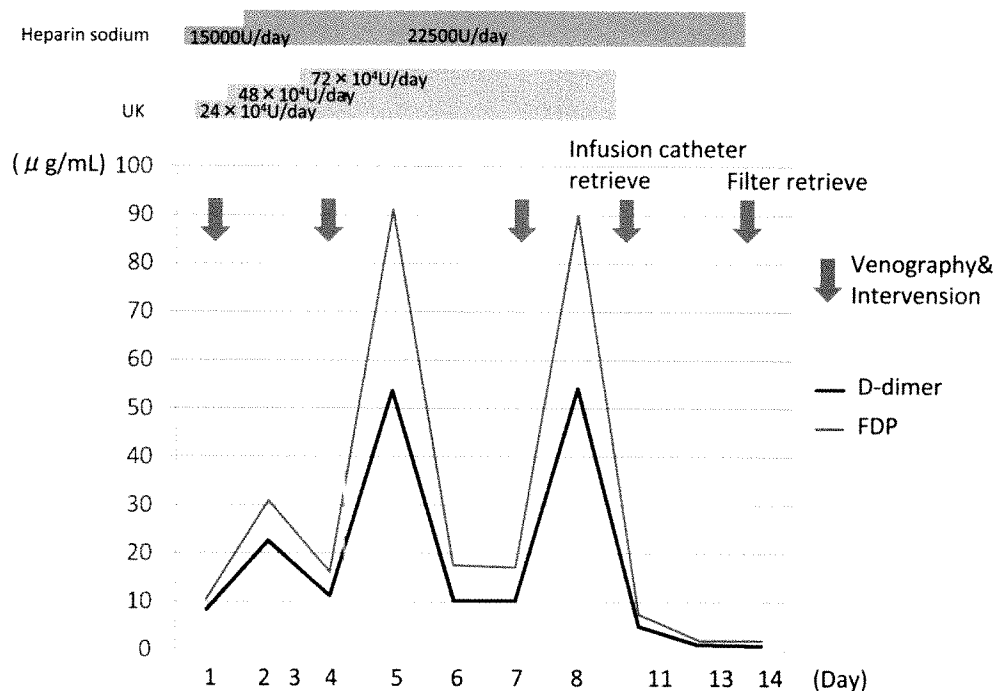


Fig. 3 On day 1, we inserted a retrievable IVC filter through his right jugular vein and placed a 20-cm pulse infusion catheter. Thrombolytic therapy by UK was started. 240000 IU UK each time was splashed out of the pulse infusion catheter twice daily for 3 days. Follow up venography on days 4 and 7 after translocation of the pulse infusion catheter and gradual tapering of the UK dose showed incomplete thrombolysis. On day 11, follow up venography showed an almost complete thrombolysis except for an organized intramural thrombus in the femoral vein, and then we retrieved the pulse infusion catheter. On the same day, we stopped the thrombolytic therapy by UK; however, we but continued the therapy with both intravenous heparin administration and intermittent pneumatic compression. On day 14, successful catheter directed thrombolysis CDT helped us retrieve the IVC filter.
IVC, inferior vena cava; UK, urokinase; CDT, catheter directed thrombolysis

Finally, CDT helped us to retrieve the IVC filter on day 14 (**Fig. 3**). During the clinical course, we didn't see any evidence of infection or bleeding complications. We had continued the therapy with both intravenous heparin administration and intermittent pneumatic compression until further improvement of motor paresis in his right leg helped him to walk unassisted. Continuous oral warfarin administration did not seem to be indispensable for the patient, because he had been free of DVT relapse for some time since the end of treatment with heparin. The patient was scheduled to receive additional chemotherapies and bone stem cell transplantation for several months after this surgery.

DISCUSSION

Original indications for the use of permanent IVC fil-

ters in patients with DVT are anticoagulant contraindications, recurrent embolism, anticoagulant complications and prophylactic use after embolectomy,⁴⁾ though others have been added recently. For preventing PTE, temporary IVC filters are reported to be as effective as permanent filters,⁵⁾ and these retrievable IVC filters have been used effectively in patients with transient risks.⁶⁾ The retrievable filters have advantages over the indwelling type because the latter can migrate, become infected or cause an infection, cause occlusion or extensive IVC thrombosis, or penetrate the aorta or vertebra.²⁾ It has been reported that *Candida* can infect an IVC filter.⁷⁾ We think that continuous oral anticoagulation therapy after insertion of an IVC filter is necessary, at least, not contraindicated. We agree with the indication of long-term continuous oral anticoagulation therapy after the insertion of an IVC filter.⁸⁾

The association between DVT and cancer has been known for a long time, and the risk of DVT is not negligible in AML patients, too.⁹⁾ Additionally, it is also undeniable that AML patients who have had a bone marrow transplant and who are on chemotherapy have an increased susceptibility to infection.

Clinical decision-making for the case reported here is as follows. When the patient was referred to the department of Cardiovascular Internal Medicine, his blood count revealed hematological complete remission. He was no longer prone to bleeding and a compromised host then. We understood that he was at high risk for fatal PE since contrast-enhanced computed tomography scanning showed massive thrombi from his right iliac vein to the femoral vein. Only a few days had passed since the onset of his clinical symptoms, and both the density of the thrombus in contrast-enhanced computed tomography and floating sign in venous ultrasonography suggested that the thrombus was unstable. For these reasons, we decided that an IVC filter was necessary in performing the CDT. Indication of a temporary use of retrievable IVC filter is under debate. We do consider evaluation of the risk for PE during CDT as important, and the routine use of an IVC filter during CDT is not indispensable. Proximal DVT, free-floating or unstable thrombus is considered to be at high risk of developing PE during CDT. Some authors have reported 32% to 60% of proximal DVT patients developed PE. However, there are complications associated with an IVC filter, such as caval occlusion, filter migration, and erosion of the IVC filter. We should consider the indication of temporary use of a retrievable IVC filter during in view of both risk evaluation of risk for PE and benefit of inserting an IVC filter. In this case, an indwelling IVC filter might take a higher risk of infection than a retrievable IVC filter in view of further treatment involving an additional two cycles of consolidation chemotherapy and a second bone marrow transplant. Considering other risks of an indwelling IVC filter and his age, we tried to perform CDT and placement of a retrievable IVC filter. We used a retrievable filter instead of a temporary filter because of two reasons. Firstly, a temporary IVC filter might decrease the activity of patient's daily life and have more infection risks because it is an external catheter. Secondly, retrievable filter can be left more safely if CDT ended in failure.¹⁰⁾ We were able to prevent fatal PTE during the acute phase, and successful CDT helped us retrieve the IVC filter, fortunately, without the patient experiencing complications of infection or bleeding. It was very important

to schedule additional cycles of consolidation chemotherapy and a second bone cell transplant. One is an infectious risk reduction, and the others are prevention of decrease in his life quality due to continuous oral anticoagulants administration and lower bleeding risks in the future. We thought that the use of a retrievable IVC filter in a young AML patient, complicated by DVT, and a later retrieval of the IVC filter after a successful CDT might reduce the risks of bleeding and infection in his further treatments for AML. To prevent DVT, we also think continuous oral anticoagulant administration is important to prevent DVT, if the patient does not have symptoms that contraindicate drug use. However, the patient was scheduled to receive additional chemotherapies within several weeks and a bone stem cell transplant after that. We did not start the oral anticoagulant administration, and there were two reasons. One was myelosuppression due to chemotherapy, and the other was a reduced risk of DVT recurrence. Myelosuppression might lead to bleeding between the additional chemotherapies before the bone stem cell transplant. First chemotherapy shrunk his extramedullary tumor and improved his motor paresis. Complete thrombus resolution due to the successful CDT and improvement of his motor paresis due to the first chemotherapy might reduce the risks of DVT recurrence.

From the outcome, we can conclude that a retrievable IVC filter with CDT may be effective and should be considered for patients at transient risk of DVT.

REFERENCES

- 1) Vijayvergiya R, Mittal BR, Grover A, Hariram V, Bhattacharya A, Singh B. Assessment of IVC filter efficacy in prevention of pulmonary thrombo-embolism by (99m) Tc-MAA lung perfusion scintigraphy-A case series and review of literature. *Int J Cardiol* 2009; **133**: 122–5.
- 2) Joels CS, Sing RF, Heniford BT. Complications of inferior vena cava filters. *Am Surg* 2003; **69**: 654–9.
- 3) Lalisie M, Willoteaux S, Negaiwi Z, Midulla M, Lions C, Beregi JP, et al. Rare complication from IVC filter: aortic and vertebral penetration. *J Radiol* 2010; **91**: 231–2.
- 4) Greenfield LJ, Cho KJ, Proctor MC, Sobel M, Shah S, Wingo J. Late result suprarenal Greenfield vena cava filter placement. *Arch Surg* 1992; **127**: 969–73.
- 5) Oshima K, Kunitomo F, Hinohara H, Ohkawa M, Saito S. The effect of a temporary inferior vena cava filter in the treatment of deep vein thrombosis in critically-ill patients. *Int Heart J* 2008; **49**: 713–21.
- 6) Rochelson B, Scher L, Warshawsky R, Simon D. Use

- of a temporary vena cava filter in a woman with septic abortion and inferior vena cava thrombosis. a case report. *J Reprod Med* 2003; **48**: 557–9.
- 7) Meda MS, Lopez AJ, Guyot A. Candida inferior vena cava filter infection and septic thrombophlebitis. *Br J Radiol* 2007; **80**: e48–9.
 - 8) Dovrish Z, Hadary R, Blickstein D, Shilo L, Ellis MH. Retrospective analysis of the use of inferior vena cava filters in routine hospital practice. *Postgrad Med J* 2006; **82**: 150–3.
 - 9) De Stefano V, Sora F, Rossi E, Chiusolo P, Laurenti L, Fianchi L, et al. The risk of thrombosis in patients with acute leukemia: occurrence of thrombosis at diagnosis and during treatment. *J Thromb Haemost* 2005; **3**: 1985–92.
 - 10) Hiromatsu S, Nata S, Ohno T, Shintani Y, Kanaya K, Sakashita H, et al. Non-permanent inferior vena cava filters for prophylaxis and treatment of lower limb venous thromboembolism. *Vasc Endovascular Surg* 2010; **44**: 668–73.

» Case Report «

Sequential Dilatation of the Superior Gluteal Artery Following Coil Embolization of the Internal Iliac Artery and Endovascular Abdominal Aneurysm Repair: A Case Report

Motoki Nakai, MD,¹ Kouhei Nakata, MD,¹ Morio Sato, MD,¹ Akira Ikoma, MD,¹ Hiroki Minamiguchi, MD,¹ Nobuyuki Kawai, MD,¹ Tetsuo Sonomura, MD,¹ Atutoshi Hatada,² Yoshiharu Nishimura,² and Yoshitaka Okamura²

We present a case of an 80-year-old male who had a right buttock claudication after embolization of the right internal iliac artery and endovascular aneurysm repair (EVAR) for aneurysms of the right common iliac and abdominal arteries. We used follow-up dynamic computed tomography to measure the diameter of the superior gluteal artery (SGA). The comparison ratio (SGA diameter after EVAR / SGA diameter before EVAR) of the right SGA at 1, 3, and 9 months was 0.74, 0.80, and 1.1, respectively, while that of the left SGA at 9 months was 0.97. The patient reported using a walking stick at 1- and 3-month follow-ups but not at the 9-month follow-up. The computed tomography (CT) showed sequential dilatation of the SGA, which appeared to be associated with the relief of the buttock claudication.

Key words: abdominal aortic aneurysm, endovascular aneurysm repair, buttock claudication, internal iliac artery

INTRODUCTION

Endovascular aneurysm repair (EVAR) has gained acceptance as a treatment for abdominal aortic aneurysms (AAA).^{1,2)} When aneurysms of the common iliac artery (CIA) and/or short length of the CIA are associated with AAA, to prevent endoleak into the AAA, it is necessary to perform coil embolization of the internal iliac artery (IIA) before EVAR for limb extension to the external iliac artery.^{3,4)} As a negative effect following coil embolization and stent graft placement for AAA, the incidence of buttock claudication is reported to be 28%–50%^{5,6)} and is dependent on symptoms that are subjec-

tively reported by the patient.

We present a case of AAA and aneurysm of right CIA that was treated by embolization of IIA and stent graft placement for AAA. After the treatment, the patient complained of buttock claudication. Symptoms gradually improved with gradual dilatation of the superior gluteal artery (SGA), as measured on follow-up contrasted computed tomography (CT).

CASE REPORT

An 80-year-old man detected a pulsating mass in his abdomen in November 2008. Ultrasound examination by his family doctor revealed AAA. Thereafter, the patient attended our hospital for EVAR in December 2008. Dynamic CT demonstrated AAA and aneurysm of the right CIA with maximum diameters of 52 and 35 mm, respectively (**Fig. 1**). The diameter and length of the proximal neck from the left renal artery to the proximal AAA end were 18.6 and 48.8 mm, respectively, and the length from the left renal artery to the terminal aorta was 125 mm. We planned to use a stent graft (Zenith, Cook, Baltimore, MD) with a diameter of 22 mm and length of 88 mm.

¹Department of Radiology, Wakayama Medical University, Wakayama, Wakayama, Japan

²Department of First Surgery, Wakayama Medical University, Wakayama, Wakayama, Japan

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Corresponding author: Morio Sato, MD. Department of Radiology, Wakayama Medical University, 811-1 Kimiidera, Wakayama, Wakayama 641-8510, Japan

Tel: +81-73-441-0604, Fax: +81-73-444-3110

E-mail: morisato@mail.wakayama-med.ac.jp



Fig. 1 Three-dimensional enhanced computed tomography using contrast medium reveals an abdominal aortic aneurysm of diameter 52 mm and a right common iliac aneurysm of diameter 35 mm.

The patient first underwent embolization of the right IIA using 17 microcoils (Tornado, Cook): 6 microcoils of 7 cm / 3 mm (length/diameter), 8 of 8 cm / 4 mm, and 3 of 10 cm / 4 mm. The microcoils were placed in the IIA trunk and branch origins of the superior and inferior gluteal arteries (**Fig. 2a**). One week later, EVAR with stent graft placement was conducted to eliminate the AAA and aneurysm of the right CIA (**Fig. 2b**). Dynamic CT immediately after EVAR demonstrated no evidence of endoleak.

Three days later, the patient suffered right hip/buttock pain after walking approximately 100 m or climbing stairs. The values of the bilateral ankle brachial index (ABI) were within the normal range (greater than 1.0). The patient was diagnosed with buttock claudication caused by EVAR.

The patient was discharged 2 weeks later, with no improvement in buttock claudication that developed during the hospital stay. The patient was followed up 1 month later and then every 2 months. Buttock claudication had improved gradually, and after 9 months, the

patient was almost free of the symptom. At 1- and 3-month follow-up visits, the patient reported that he required a walking stick, though he reported at the 9-month follow-up visit that it was no longer required. The state of the AAA, CIA aneurysm, and bilateral SGAs was monitored using dynamic CT (multi-slice CT with 16 detectors: Aquilion 16, Toshiba, Tokyo, Japan). Dynamic CT was obtained from the upper abdomen to the lower pelvis, with intravenous administration of contrast medium (Iopamiron 300, Bayer Schering Pharma, Berlin, Germany) at a rate of 3 mL/s (total dose, 100 mL) using an automatic power injector. The diameters of the right SGA measured on dynamic CT before EVAR, and at 1, 3, and 9 months after EVAR, were 5.3, 3.8, 4.2, and 5.8 mm, respectively (**Fig. 3**), while those of the left SGA before EVAR and at 9 months after were 5.75 and 5.60 mm, respectively. The comparison ratio (diameter of the SGA after EVAR / that before EVAR) of the right buttock at 1, 3, and 9 months was 0.74, 0.80, and 1.1, respectively, while that of the left buttock at 9 months was 0.97. Dynamic CT at 9 months after EVAR revealed dilated SGA and its branch arteries (**Fig. 3**). An improvement in the right buttock claudication was dependent on the degree of dilatation of the right SGA.

DISCUSSION

In cases of AAA associated with aneurysm involvement of the CIA or with a short CIA, coil embolization of the ipsilateral IIA before stent graft placement is indicated to prevent endoleak.^{3, 4)} Buttock claudication, erectile disturbance, and colon ischemia are listed as complications after IIA embolization. The frequency of buttock claudication is reported as 28%–50% after embolization of the ipsilateral IIA^{5, 6)} and as 31%–80% after embolization of bilateral IIAs.^{6, 7)} In addition, the embolization site determines the frequency of buttock claudication: frequency is reported to be 13% for embolization of the IIA trunk alone, and 66.6% for simultaneous embolization of the IIA trunk and branches of the superior and inferior gluteal arteries.⁸⁾ In the present case, embolization of the IIA trunk, SGA, and inferior gluteal artery resulted in buttock claudication. To avoid interruption of blood flow from the contralateral IIA, we must embolize the IIA trunk alone (**Fig. 4**). Balloon inflation at the origin of the IIA, the use of a detachable coil as an anchor or both used together are preferable techniques for IIA trunk embolization because they avoid migration of embolic materials into the peripheral branches.



Fig. 2 Pelvic angiography after embolization of the right internal iliac artery with microcoils shows aortic and right common iliac artery aneurysms (a). One week later, endovascular placement of a Zenith stent graft was performed. Abdominal aortography reveals elimination of the abdominal aortic and right common iliac artery aneurysms, without endoleak (b).

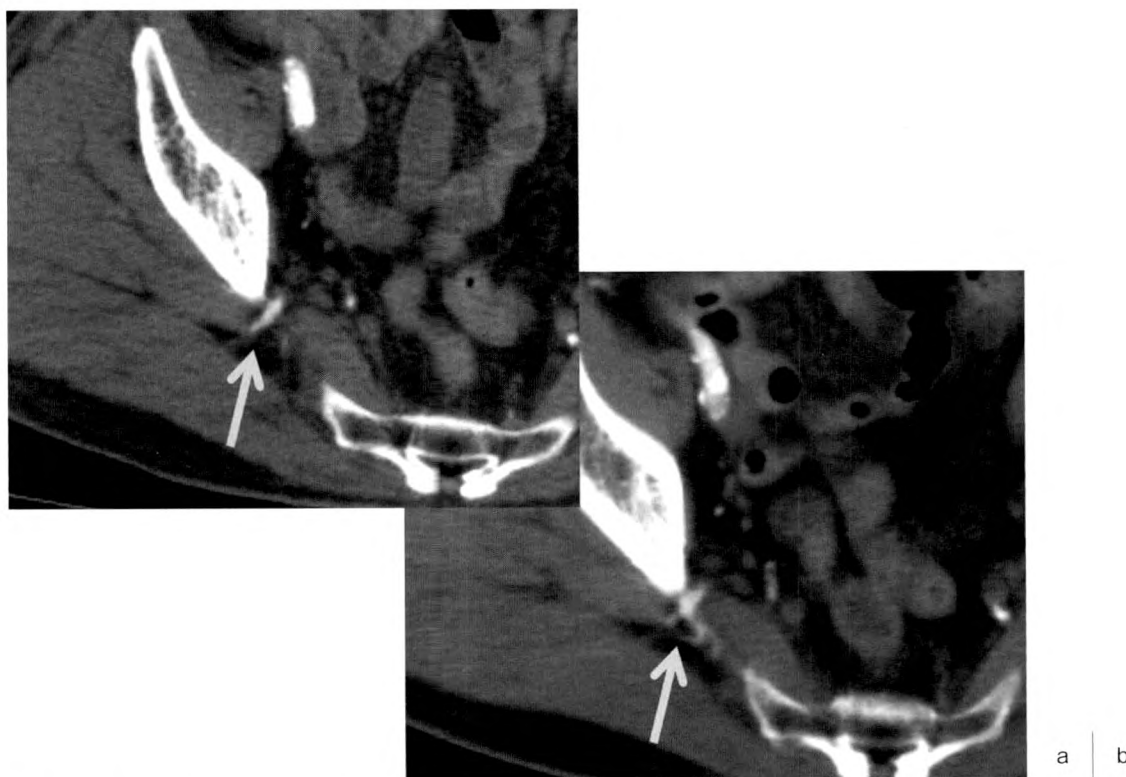


Fig. 3 Enhanced computed tomography at the level of the superior gluteal artery. The diameters of the superior gluteal artery (arrow) after 1 month (a) and 9 months (b) endovascular aneurysm repair was 3.8 and 5.8 mm, respectively. Dilated superior gluteal branch arteries were also visualized 9 months after repair (b).

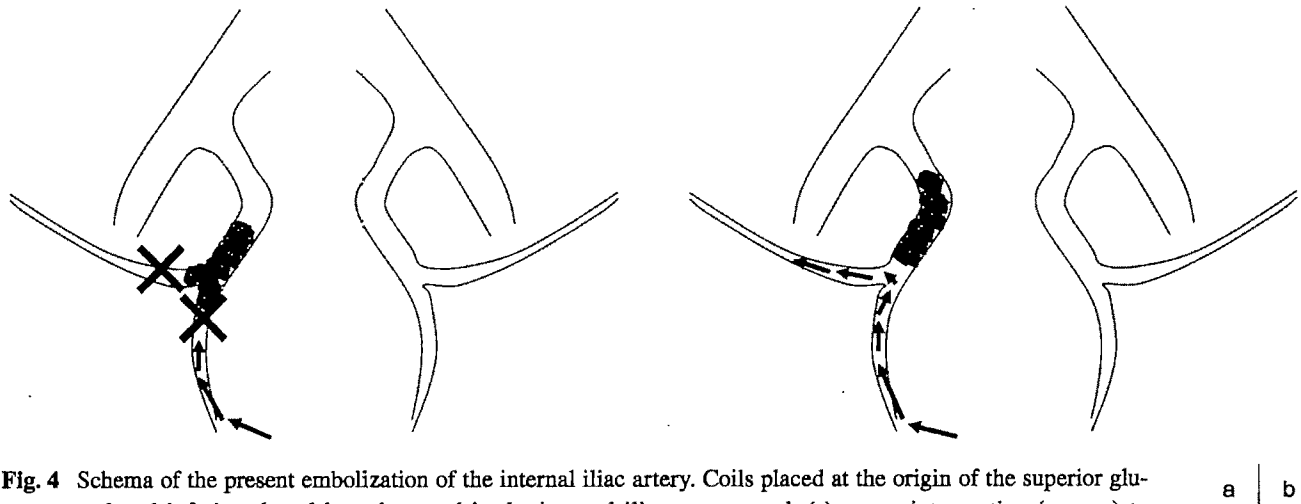


Fig. 4 Schema of the present embolization of the internal iliac artery. Coils placed at the origin of the superior gluteal and inferior gluteal branches, and in the internal iliac artery trunk (a), cause interruption (crosses) to blood flow (arrows) from the contralateral iliac artery, resulting in a possible decrease in blood flow to the gluteal muscle. A schema of our recommended embolization of the internal iliac artery (b) would possibly preserve the blood supply (arrows) from the contralateral internal iliac artery.

It is reported that buttock claudication is relieved within 3–6 months in the majority of cases, and in more than 6 or 12 months in some cases.^{5,7)} In the present case, buttock claudication eased over a period of 9 months, as reported by the patient. The relief of buttock claudication is considered to be dependent on the development of collateral arteries. However, the presence of newly developed collateral arteries cannot yet be confirmed by imaging. Follow-up dynamic CT demonstrated gradual dilatation of the ipsilateral SGA and its branch arteries with time, and dilatation of the ipsilateral SGA was objectively confirmed by measuring the SGA diameter. ABI is an objective indicator for ischemia of the lower extremities but not for buttock ischemia. In the present case, an increase in SGA diameter seems to be associated with an improvement in buttock claudication.

The major collateral pathways that function after an IIA embolization are provided by the contralateral IIA, the ipsilateral lumbar artery, and the ipsilateral deep femoral artery (lateral and medial femoral circumflex artery).^{9, 10)} In the present case, buttock claudication did not occur after the IIA embolization; however, it did occur after stent graft placement and then IIA embolization, which improved after 9 months. The collateral pathway between the lateral femoral circumflex artery and the SGA exists as one of the major anastomotic channels. We consider that simultaneous embolization of the IIA trunk and the superior and inferior gluteal arteries interrupts the blood flow from the contralateral IIA and that

stent graft placement interrupts the increased blood flow from the lumbar artery caused by IIA embolization, resulting in prominent buttock claudication; gradual development of other collateral pathways, including the femoral circumflex artery, then leads to relief of the claudication.

In conclusion, we presented a case of AAA and CIA aneurysm treated with simultaneous embolization of the IIA trunk, and the superior and inferior gluteal arteries, followed by stent graft placement, resulting in buttock claudication. Ideally, embolization of the IIA trunk alone should be performed to preserve the blood flow from the contralateral IIA. The dilatation of the SGA was observed on follow-up CT, and sequential dilatation of SGA appeared to be associated with the relief of the buttock claudication.

DISCLOSURE STATEMENT

We declare no financial support or conflicts of interest and record no acknowledgements.

REFERENCES

- 1) Brewster DC, Cronenwett JL, Hallett JW Jr, Johnston KW, Krupski WC, Matsumura JS, et al. Guidelines for the treatment of abdominal aortic aneurysms. Report of a subcommittee of the Joint Council of the American Association for Vascular Surgery and Society for Vascular Surgery. *J Vasc Surg* 2003; **37**: 1106–17.

- 2) Prinssen M, Verhoeven EL, Buth J, Cuypers PW, van Sambeek MR, Balm R, et al. A randomized trial comparing conventional and endovascular repair of abdominal aortic aneurysms. *N Engl J Med* 2004; **351**: 1607–8.
- 3) Criado FJ, Wilson EP, Velazquez OC, Carpenter JP, Barker C, Wellons E, et al. Safety of coil embolization of the internal iliac artery in endovascular grafting of abdominal aortic aneurysms. *J Vasc Surg* 2000; **32**: 684–8.
- 4) Kickuth R, Dick F, Triller J, Ludwig K, Schmidli J, Do DD. Internal iliac artery embolization before endovascular repair of aortoiliac aneurysms with a nitinol vascular occlusion plug. *J Vasc Interv Radiol* 2007; **18**: 1081–7.
- 5) Razavi MK, DeGroot M, Olcott C 3rd, Sze D, Kee S, Semba CP, et al. Internal iliac artery embolization in the stent-graft treatment of aortoiliac aneurysms: analysis of outcomes and complications. *J Vasc Interv Radiol* 2000; **11**: 561–6.
- 6) Schoder M, Zaunbauer L, Hölzenbein T, Fleischmann D, Cejna M, Kretschmer G, et al. Internal iliac artery embolization before endovascular repair of abdominal aortic aneurysms: frequency, efficacy, and clinical results. *AJR Am J Roentgenol* 2001; **177**: 599–605.
- 7) Bratby MJ, Munneke GM, Belli AM, Loosemore TM, Loftus I, Thompson MM, et al. How safe is bilateral internal iliac artery embolization prior to EVAR? *Cardiovasc Intervent Radiol* 2008; **31**: 246–53.
- 8) Kritpracha B, Pigott JP, Price CI, Russell TE, Corbey MJ, Beebe HG. Distal internal iliac artery embolization: a procedure to avoid. *J Vasc Surg* 2003; **37**: 943–8.
- 9) Barksdale PA, Elkins TE, Sanders CK, Jaramillo FE, Gasser RF. An anatomic approach to pelvic hemorrhage during sacrospinous ligament fixation of the vaginal vault. *Obstet Gynecol* 1998; **91**: 715–8.
- 10) Chait A, Moltz A, Nelson JH Jr. The collateral arterial circulation in the pelvis. An angiographic study. *Am J Roentgenol Radium Ther Nucl Med* 1968; **102**: 392–400.

► Case Report ◀

Iatrogenic Arteriovenous Fistula as a Cause for Leg Ulcers: A Case Report

Kurian J Mylankal,¹ Brian Johnson,² and Duncan F Ettles³

An 80-year-old man presented with painful leg ulceration due to steal phenomenon from a groin arteriovenous fistula (AVF) 10 years following a coronary angiogram. The diagnosis of the AVF was confirmed by duplex examination of the groin vessels which demonstrated characteristic flow pattern in the femoral arterial and venous system. Angiography further confirmed the site of the fistulous communication and this was managed by a covered stent graft. We discuss the incidence of AVF, risk factors for its development, relevant diagnostic investigations and management options along with strategies to reduce the incidence of AVF following percutaneous punctures.

Key words: arteriovenous fistula, duplex, leg ulcers, percutaneous puncture

INTRODUCTION

Arteriovenous fistulae are an abnormal communication between the artery and vein arising commonly following penetrating injury such as percutaneous arterial or venous punctures and after open surgical interventions.¹ They are encountered in the groin due to frequent use of the femoral artery and vein for diagnostic and interventional radiological procedures such as coronary and peripheral angiography.

In the acute phase, arteriovenous fistulae are commonly associated with localized symptoms such as haematoma and bruising. However, they may remain totally asymptomatic and present in the long term with chronic limb oedema, aneurysmal degeneration of the arterial tree and high output cardiac failure. This case report dis-

cusses a unique case of an arteriovenous fistula in the groin in a patient presenting with painful lower limb ulcerations, which has not been reported in the literature previously. The investigations leading to confirmation of the diagnosis and the subsequent management of the fistula are also discussed along with a brief review of the literature.

CASE REPORT

An 80 year old male patient presented to the vascular clinic with a two-year history of painful right leg ulcers, which were resistant to healing by a conservative dressing regime. There was no history of trauma prior to the onset of ulcerations and there were no medical risk factors for peripheral arterial disease. However, he had undergone a coronary angiogram via the right femoral artery puncture over 10 years ago. The procedure was uncomplicated with no immediate complications recorded.

The clinical examination revealed superficial ulcerations in the right lower calf area with varicose veins in the long saphenous vein distribution. There was a palpable right femoral pulse with absent popliteal and foot pulses. However, the left lower limb had a full complement of femoral and distal pulses. In addition; on auscultation, a bruit was audible in the right groin.

Subsequently, the patient underwent a duplex scan of

¹Department of Vascular and Endovascular Surgery, Fremantle Hospital, Western, Australia

²Academic Vascular Unit, Hull Royal Infirmary, Hull, United Kingdom

³Department of Radiology, Hull Royal Infirmary, Hull, United Kingdom

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Corresponding author: KJ Mylankal. Department of Vascular and Endovascular Surgery, Fremantle Hospital, Alma Street, Fremantle, 6160, Western, Australia
Tel: +61-435588174, Fax: +61-894312009
E-mail: kjmylankal@yahoo.co.uk



Fig. 1 AVF between the Right profunda artery and common femoral vein.
AVF, arteriovenous fistula

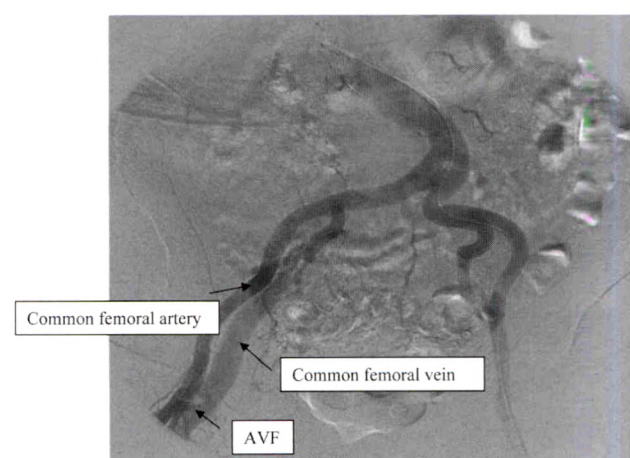


Fig. 2 Left retrograde intra-arterial digital subtraction angiography.
AVF, arteriovenous fistula

the right lower limb. The right common femoral and profunda artery demonstrated loss of triphasic flow with continuous forward flow in diastole with no reversal of flow in diastole. In addition, an arteriovenous fistula with a high velocity jet stream of blood was visualized between the profunda femoris artery and common femoral vein (Fig. 1).

To delineate the anatomy and assess suitability for endovascular intervention, the patient underwent a retrograde intra-arterial digital subtraction angiogram via left femoral puncture using a 6 Fr vascular sheath and pigtail

catheter. This demonstrated early contrast filling of the right iliac venous system, suggesting a communication between the arterial and venous system (Fig. 2). In addition, selective cannulation of the right profunda and superficial femoral arteries revealed two separate fistulae originating from the superficial femoral artery and profunda femoris artery, both communicating with the common femoral vein. After an initial diagnostic angiography, a 7 Fr guiding sheath (Destination Guiding sheath, Terumo, Europe) was introduced via the left common femoral artery and placed across the aortic bifurcation to the right external iliac artery by the up and over approach. Selective angiography revealed two separate fistulae originating from the superficial femoral artery and profunda femoris artery, both communicating with the common femoral vein. A bolus of 3000 iu of heparin was administered via the sheath. With road-map assistance, the superficial femoral artery was catheterized using an angled hydrophilic guidewire (Standard Glidewire®, Terumo Medical Corporation) and exchanged for a 0.035 inch stiff guide wire (Amplatz Super Stiff, Boston Scientific, USA) over a straight exchange catheter. After calibrating the vessel diameter and using road-map guidance, a 4 to 9-mm Jomed covered stent (Jomed, Rangendingen, Netherlands) mounted on a 6 mm balloon was accurately deployed across the arteriovenous fistula (AVF). The profunda femoris artery was next cannulated and a 4 to 9-mm Jomed covered stent (Jomed, Rangendingen, Netherlands) on a 5-mm balloon was deployed over the AVF defect in the profunda femoris artery. A final check angiography confirmed a satisfactory position of the stents with exclusion of both fistulae (Fig. 3). A vascular closure device (6 Fr Angio-Seal™, St Jude Medical) was used to seal the left femoral artery puncture site. These were amenable to endovascular treatment by placing a covered stent over the fistulous defect and thus avoiding an open surgical procedure (Fig. 3). The patient was subsequently discharged on the second day following the procedure with no immediate complications. There was a significant improvement in the right leg ulcerations on subsequent review in the vascular clinic with an ankle brachial pressure index of 0.8 from a pre intervention recording of 0.37.

DISCUSSION

Arteriovenous fistula occur following penetrating injuries such as percutaneous interventions, surgical procedures and venous catheterization although they can

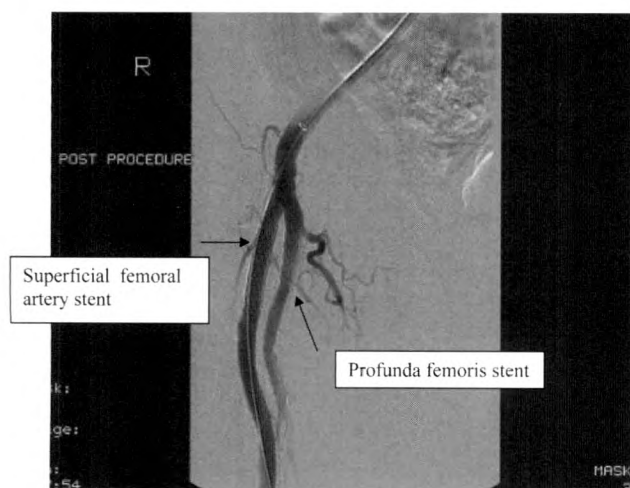


Fig. 3 Stents deployed in the right profunda and superficial femoral artery.

rarely present after blunt trauma.²⁾ The overall incidence of arteriovenous fistula following percutaneous femoral puncture for cardiac catheterization is 1%.³⁾ The risk factors for arteriovenous fistula formation following percutaneous femoral puncture from multivariate analysis were use of anticoagulation, arterial hypertension, female gender, puncture of superficial femoral or profunda artery and left groin puncture.^{4, 5)}

AVF may be relatively asymptomatic with bruising and small haematomas in the acute phase attributed to the percutaneous intervention. However chronic arteriovenous fistula may present with symptoms of intermittent claudication due to the steal phenomenon. Iliac and femoral artery aneurysms occur due to increased flow of blood through the arterial tree due to short circuiting of the blood. Venous hypertension and high output cardiac failure are also a consequence of this increased handling of high-volume blood flow.^{2, 6)}

The diagnosis of arteriovenous fistula is by clinical findings of bruit in conjunction with corroborating history. However, a bruit may not always be detected clinically, especially when the arteriovenous fistula is deep within the tissues. Due to the steal phenomenon, blood flow to the extremities may be compromised, as evidenced by reduced or absent distal peripheral pulses. Patients may present with intermittent claudication. Although critical limb ischaemia, resulting in ischaemic ulceration is possible with a significant steal, this has not been reported in the literature previously.

Duplex imaging is diagnostic for arteriovenous fistula and offers the advantage of a non-invasive investigation.

The waveform is characteristically high volume, monophasic with turbulence and the jet stream, visualized by the color aliasing. It gives dynamic information of the site of the arteriovenous fistula in addition to the grade of steal into the venous system. It is a diagnostic investigation for peripheral arteriovenous fistula. Intra-arterial digital subtraction angiography has the advantage of high specificity and helps localize the arteriovenous fistula by selective cannulation of the vessel.

The management of arteriovenous fistula is multimodal. Non-invasive management with manual pressure applied using an ultrasound probe or simple prolonged bandaging have been proven to be effective and economical.^{7, 8)} One third of all arteriovenous fistula close spontaneously in one year, and hence, there is some evidence to manage asymptomatic arteriovenous fistula conservatively by a wait and watch policy before initiating any treatment.⁴⁾

Endovascular techniques have the advantage of being a minimally invasive intervention with reduced patient morbidity and in-patient stay. Covered stents help exclude the fistula from the arterial blood flow and thus results in thrombotic occlusion of the fistula.⁹⁻¹¹⁾ In addition, there is also the option of using glue to occlude the fistula by selective catheterization of the affected vessel.¹²⁾

Surgical management is reserved for arteriovenous fistulae that are symptomatic and fail treatment by non-invasive techniques. It is the gold standard and involves identification of the fistula, resecting it and repair of the artery. Although it has a high success rate of over 96%, there are potential complications of major bleeding from the arterialized vein, groin infection and scarring.^{13, 14)}

The complication of arteriovenous fistula resulting from percutaneous procedures can be minimized by various precautionary measures. The use of an ultrasound-guided, central venous line cannulation has been recognized as a safe technique to reduce complications. Similarly, there is emerging evidence to demonstrate that the use of ultrasound-guided femoral puncture reduces the incidence of complications such as arteriovenous fistula, false aneurysm formation and haematoma. Ultrasound helps determine the level of bifurcation of the common femoral artery and thus avoids the inadvertent puncture of the superficial femoral or profunda artery. The latter are well identified risk factors for arteriovenous fistula formation.¹⁾

The use of fluoroscopy to mark the head of the femur, which is also a reliable anatomical landmark for bifurcation of the common femoral artery, has been demonstrated

to be a safe technique to avoid puncture of the superficial femoral artery and profunda artery.⁵⁾

Commercially available vascular closure devices are increasingly being used in the clinical practice due to their convenience and ease of use. These devices are introduced intra-luminally and deploy a seal or ligature over the arterial puncture site. There is evidence to suggest that these devices, when used appropriately, help reduce the complications associated with percutaneous puncture.¹⁵⁾

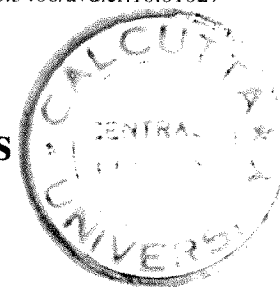
REFERENCES

- 1) Straton CS, Tisnado J. Spontaneous arteriovenous fistulas of the lower extremities: angiographic demonstration in five patients with peripheral vascular disease. *Cardiovasc Intervent Radiol* 2000; **23**: 318-21.
- 2) Kotelis D, Klemm K, Tengg-Koblick H, Allenberg JR, Böckler D. Intermittent claudication secondary to a traumatic arteriovenous fistula. *Vasa* 2007; **36**: 285-7.
- 3) Perings SM, Kelm M, Jax T, Strauer BE. A prospective study on incidence and risk factors of arteriovenous fistulae following transfemoral cardiac catheterization. *Int J Cardiol* 2003; **88**: 223-8.
- 4) Kelm M, Perings SM, Jax T, Lauer T, Schoebel EC, Heintzen MP, et al. Incidence and clinical outcome of iatrogenic femoral arteriovenous fistulas: implications for risk stratification and treatment. *J Am Coll Cardiol* 2002; **40**: 291-7.
- 5) Kim D, Orron DE, Skillman JJ, Kent KC, Porter DH, Schlam BW, et al. Role of superficial femoral artery puncture in the development of pseudoaneurysm and arteriovenous fistula complicating percutaneous transfemoral cardiac catheterization. *Cathet Cardiovasc Diagn* 1992; **25**: 91-7.
- 6) Melliére D, Barres G, Saada F, Becquemin JP. Late arterial aneurysm proximal to corrected post-traumatic arteriovenous fistula. *J Cardiovasc Surg (Torino)* 1987; **28**: 510-5.
- 7) Wery D, Delcour C, Golzarian J, Azancot M, Grand C, Struyven J. [Iatrogenic femoral pseudo-aneurysm and arteriovenous fistula. Non-surgical treatment]. *J Radiol* 1991; **72**: 91-4.
- 8) Zhou T, Liu ZJ, Zhou SH, Shen XQ, Liu QM, Fang ZF, et al. Treatment of postcatheterization femoral arteriovenous fistulas with simple prolonged bandaging. *Chin Med J (Engl)* 2007; **120**: 952-5.
- 9) Cil BE, Akmangit I, Peynircioglu B, Karçaaltincaba M, Cekirge S. Iatrogenic femoral arteriovenous fistula: endovascular treatment with covered stent implantation and 4-year follow-up. *Diagn Interv Radiol* 2006; **12**: 50-2.
- 10) O'Brien J, Buckley O, Torreggiani W. Hemolytic anemia caused by iatrogenic arteriovenous iliac fistula and successfully treated by endovascular stent-graft placement. *AJR Am J Roentgenol* 2007; **188**: 306.
- 11) Onal B, Kosar S, Gumus T, Ilgit ET, Akpek S. Postcatheterization femoral arteriovenous fistulas: endovascular treatment with stent-grafts. *Cardiovasc Intervent Radiol* 2004; **27**: 453-8.
- 12) Onal B, Ilgit ET, Akpek S, Coskun B. Postcatheterization femoral arteriovenous fistula: endovascular treatment with N-butyl-cyanoacrylate embolization. *Cardiovasc Intervent Radiol* 2006; **29**: 276-8.
- 13) Parodi JC, Schonholz C, Ferreira LM, Bergan J. Endovascular stent-graft treatment of traumatic arterial lesions. *Ann Vasc Surg* 1999; **13**: 121-9.
- 14) Linder F. Acquired arterio-venous fistulas. Report of 223 operated cases. *Ann Chir Gynaecol* 1985; **74**: 1-5.
- 15) Jaff MR, Hadley G, Hermiller JB, Simonton C, Hinojara T, Cannon L, et al. The safety and efficacy of the StarClose Vascular Closure System: the ultrasound substudy of the CLIP study. *Catheter Cardiovasc Interv* 2006; **68**: 684-9.

» Case Report «

Fibromuscular Dysplasia of the Lower Extremities

Jin Okazaki, MD, PhD, Atsushi Guntani, MD, Kenichi Homma, MD, Ryoichi Kyuragi, MD, Eisuke Kawakubo, MD, and Yoshihiko Maehara, MD, PhD



Fibromuscular dysplasia (FMD) is a nonatherosclerotic, non-inflammatory vascular disease that mainly affects the renal and internal carotid arteries. Involvement of other sites, including arteries of the extremities, is uncommon, and only a few histologically confirmed cases have been reported. FMD of the arteries of the extremities can result in ischemia requiring surgical or endovascular reconstruction. In the present report, two cases of FMD are described: one case of femoropopliteal artery occlusive disease, and one case of nonsymptomatic progression of external iliac artery dissection, both with histological confirmation of FMD. Clinical presentation, treatment, outcome and histological findings of previously reported cases are reviewed. FMD should be considered as a cause of occlusion, stenosis, dissection or aneurysm of the peripheral arteries: although rare, it can lead to limb-threatening ischemia or life-threatening aneurysm rupture.

Key words: fibromuscular dysplasia, femoral artery, iliac artery, dissection, aneurysm, extremity

INTRODUCTION

Fibromuscular dysplasia (FMD) is a nonatherosclerotic, non-inflammatory systemic occlusive arteriopathy of unknown etiology that mainly affects renal, carotid, and splanchnic arteries. Since it was first described in 1938,¹⁾ numerous reports have appeared describing the disease both in renal arteries and extra-renal vessels.²⁾ Involvement of the arteries of the extremities is uncommon, and only a few histologically confirmed cases have been reported. FMD-related lesions in the extremities occasionally cause limb ischemia through luminal stenosis or peripheral thrombus. Aneurysm formation caused by FMD may also cause limb ischemia through peripheral thrombus. This ischemia can be resolved with arterial reconstruction.

Department of Surgery and Science, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Fukuoka, Japan

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Corresponding author: Jin Okazaki, Department of Surgery and Science, Graduate School of Medical Sciences, Kyushu University, 3-1-1 Maidasi, Higashi-ku, Fukuoka, Fukuoka 812-0054, Japan

Tel: +81-92-642-5466, Fax: +81-92-642-5482

E-mail: jokazaki@surg2.med.kyushu-u.ac.jp

REPORT OF CASES

Case 1

Clinical findings

A 63-year-old woman presented with disabling left leg claudication, along with hypertension and hypercholesterolemia treated by oral medication. Physical examination revealed a pulsating mass in the lower abdomen, normal pulses over the femoral arteries, a bilateral pulsating mass on the popliteal arteries, and no pulsation over the left pedal artery. The left foot was cold with skin pallor. Ankle-brachial pressure indices were 0.37 on the left and 0.75 on the right. Laboratory values upon admission included serum cholesterol of 396 mg/dl and triglycerides of 674 mg/dl. Three-dimensional computed tomography (CT) revealed bilateral common iliac artery aneurysms (measuring 5.9 cm in the left and 4.0 cm in the right), and serial stenoses altering with mural aneurysms in bilateral superficial femoral and popliteal arteries (the classic “string-of-beads” appearance) (**Fig. 1**). Popliteal arteries presented with aneurysms (measuring 17 mm in the left and 20 mm in the right) with luminal thrombi. The left popliteal artery was occluded above the trifurcation, and only the peroneal artery was contrast enhanced through collateral vessels. On the right side,

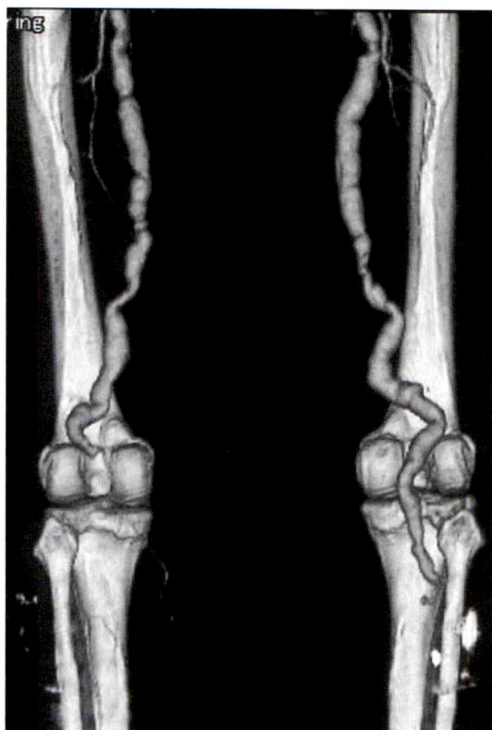


Fig. 1 Computed tomographic angiography of case 1. “String-of-beads” appearance on bilateral the femoral and popliteal arteries.

the lumen of the right popliteal aneurysm was patent, the tibioperoneal trunk was occluded, and only the anterior tibial artery was patent. There were no abnormal findings on the renal or visceral arteries, although the “string-of-beads” appearance was observed bilaterally in the internal carotid arteries. From the characteristic “string-of-beads” appearance, FMD of bilateral femoropopliteal and internal carotid arteries, and bilateral common iliac and bilateral popliteal artery aneurysms were diagnosed.

The iliac aneurysms were successfully excised and reconstructed with a Y graft. After 1 month, left leg ischemia was treated with a femoral to peroneal artery bypass with a reversed great saphenous vein. The superficial femoral artery was ligated at its origin, and its short segment was excised for histological examination. The postoperative course was uneventful.

Histological findings

The medial layer of the femoral artery was thickened by marked collagen fibrosis and muscular hyperplasia. Smooth muscle fibers were focally disorganized, and internal elastic membrane was partially fragmented. Intima contained marked fibrous thickening and a focus of atheromatous gruel (Fig. 2). Findings were compatible



Fig. 2 Femoral artery of case 1 in cross-section. Medial layer is focally thickened with marked collagen fibrosis and disorganized muscular hyperplasia. Internal elastic membrane is partially fragmented. Intima also shows a marked fibrous thickening and focus of atheromatous gruel. (elastic van Gieson stain, original magnification $\times 40$)

with medial fibroplasia with associated atherosclerotic change caused by aging and hyperlipidemia.

Case 2

Clinical findings

A 37-year-old man presented with sudden-onset back pain. No clinical features suggestive of Marfan or Ehlers-Danlos syndrome were present. Although the patient reported no history of vascular events, he had a family history of maternal death at 60 years of age by rupture of an aneurysm. Because CT revealed the presence of a retroperitoneal hematoma surrounding the body of the pancreas, acute pancreatitis was diagnosed and the treatment with intravenous administration of protease inhibitor was initiated. Thereafter, detailed CT findings suggested dissection and rupture and spontaneous thrombus of the celiac artery (Fig. 3). Percutaneous transluminal coil embolization of the partially thrombosed celiac trunk was successfully conducted. Systemic vascular investigation revealed a short segment of dissection in the right external iliac artery. The renal, cerebral, and peripheral arteries appeared normal. No symptoms of lower leg ischemia were present initially. After follow-up by three-dimensional CT for 17 months, the right iliac dissected lumen was enlarged, and a new dissection appeared in the left external iliac artery (Fig. 4). Resection and interposition of bilateral external iliac arteries with ePTFE prosthetic grafts were performed.

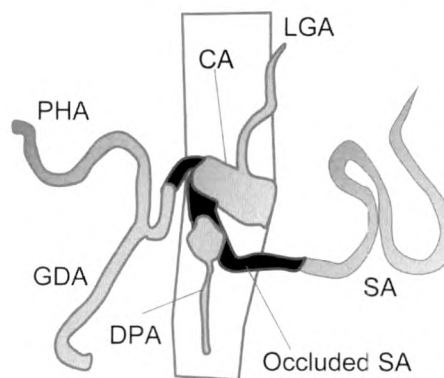


Fig. 3 Computed tomographic angiography of case 2. Dissected celiac artery with segmental thrombosis. Partially patent lumen of splenic artery was contrast enhanced through posterior pancreatic artery.
CA, celiac artery; SA, splenic artery; PHA, proper hepatic artery; GDA, gastroduodenal artery; LGA, left gastric artery; DPA, dorsal pancreatic artery

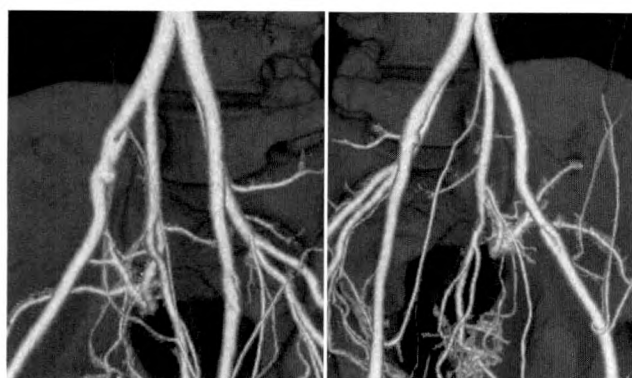


Fig. 4 Computed tomographic angiography of case 2. Dissections in right (A) and left (B) external iliac arteries.



Fig. 5 Macroscopic luminal view of resected external iliac artery in case 2. Dissection and unusual corrugations by serial wall thickening and the intervening crease are visible.

Luminal visualization of the resected external iliac arteries revealed dissection and unusual corrugations by serial wall thickening and an intervening crease (**Fig. 5**). The postoperative course was uneventful.

Histological findings

External iliac artery cross-section revealed both intimal and medial thickening and medial dissection. Intimal layer had irregularly arranged mesenchymal cells present in a loose matrix of fibrous connective tissue. No lipid or inflammatory components were present. The inner media was thickened with disoriented smooth muscle fibers, and the internal elastic membrane was partially fragmented. A dissected channel was present at the outer third of the media, dividing the medial layer into a fibroplastic inner

layer and an almost intact paramedial layer. External elastic membrane and adventitia were almost intact (**Fig. 6**). Findings were compatible with medial dissection with concomitant secondary intimal fibroplasia.

DISCUSSION

Fibromuscular dysplasia is a group of nonatherosclerotic, non-inflammatory arteriopathy that most commonly involve renal and carotid arteries, though it has been described in almost every arterial bed in the body. The clinical presentation may vary from an asymptomatic condition to a limb-threatening ischemia or life-threatening hemorrhage, depending on the involvement of the arterial bed, degree of stenosis, and pathological

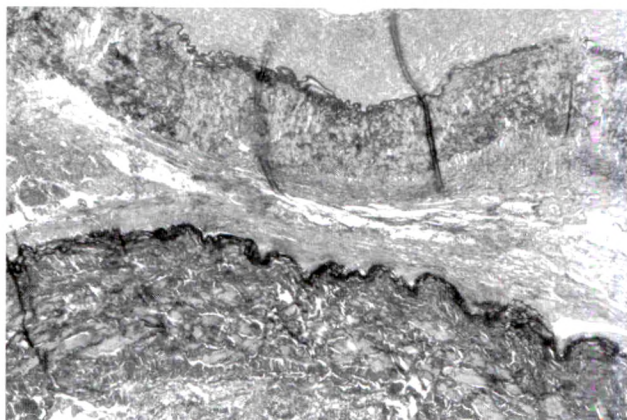


Fig. 6 External iliac artery of case 2 in cross-section. A dissected channel is present at the outer third of media, dividing the medial layer into a fibroplastic inner part and an almost intact perimedial part. Intima is also thickened with irregularly arranged mesenchymal cells. (elastic van Gieson stain, original magnification $\times 40$)

types of FMD.

A pathological classification of FMD was proposed by Harrison and McCormack according to the vessel layer involved; i.e., medial, intimal, and adventitial.³⁾ Medial fibromuscular dysplasia is most common (85%) and has been defined further into four subgroups: medial fibroplasia, perimedial fibroplasia, medial hyperplasia, and medial dissection.

Medial fibroplasia occurs most frequently and is well known because of the “string-of-beads” appearance on angiography. This appearance is the result of focal areas of stenosis with intervening areas of aneurysmal dilatation. Stenotic areas are due to thickened fibromuscular ridges, in which the arterial muscle is completely replaced by fibroplasia with loose collagen. The mural aneurysm results from thinning or complete loss of smooth muscle. The internal elastic membrane is deficient in the aneurysms.

In medial hyperplasia, the stenosis is produced primarily by hyperplasia of arterial smooth muscle cells.

In medial dissection, a channel is located on the outer third of the media. The media displays zones of fibroplasia replacing degenerated elastic fibrils, particularly around the channel.

Perimedial fibroplasia is characterized by marked, intense fibroplasia in the outer half of the media which usually replace the external elastic membrane. The fibroplastic layer varies in thickness, so considerable irregularity of the lumen is produced.

Intimal fibroplasia occurs in less than 10% of patients

with FMD and is characterized by an accumulation of loose, moderately cellular fibrous tissue without atherosclerotic or inflammatory components. Blunt trauma, catheter-induced intraluminal injury, or luminal stenosis of the vessel may cause “secondary” intimal fibroplasia.

Adventitial fibroplasia is the least common in the renal FMD and, to our knowledge, has never been reported in extremity arteries.

Using the Harrison and McCormack classification, case 1 was diagnosed as medial fibroplasia with added atherosclerotic change; case 2 was diagnosed as medial dissection with secondary intimal fibroplasia. Without a histological diagnosis, we are not certain if the celiac arterial dissection in case 2 was caused by FMD, although FMD could occasionally occur in visceral arteries, and there are some reports describing celiac artery dissection caused by FMD, with a histological diagnosis.⁴⁾

The etiology of FMD has been the subject of much speculation. Cigarette smoking is associated with an increased risk of this disease; however, the mechanisms by which smoking contributes to the development of FMD have not been elucidated. The predominance of the disease in middle-aged women has led to the suggestion that it is caused by a hormonal influence on smooth muscle. Mechanical vessel wall stress is another classical hypothesis, as FMD of the renal arteries often co-presents with ptosis of the right kidney. Sang et al. analyzed these environmental factors in a case-control study of 33 patients with FMD. The number of pregnancies, oral contraceptives, gynecological disorders, and incidence of abnormal renal mobility did not differ between patients with FMD and matched controls.⁵⁾ Genetic factors may also play a role in FMD, and since the disease is more common among first-degree relatives,⁶⁾ an autosomal dominant transmission of the disease has been suggested.^{7, 8)} Some inheritable connective tissue disorders, such as Ehlers-Danlos syndrome (type IV)⁹⁾ and Marfan syndrome,¹⁰⁾ are associated with multiple aneurysms and arterial dissection and have been associated with FMD. Bofinger et al. reported a significantly higher frequency of angiotensin-converting enzyme I allele in FMD patients than in controls¹¹⁾ and suggested that a polymorphism of the renin-angiotensin system may cause defective remodeling in the muscular layer of arteries and subsequent development of FMD. Autoimmunity associated with HLA Drw6 was also suggested in a limited study.⁵⁾ Because of the lack of large cohorts, these studies on the possible causes of FMD have not been confirmed.

Numerous reports have described FMD occurring in

Table 1 FMD in femoral and popliteal arteries

Author (year)	Age	Sex	Site of disease	Appearance	Presentation	Treatment	Outcome	Histology
Prince and Vawter (1971)	1	M	Bilateral femoral arteries	Beaded	Ischemia	Amputation	Amputation	Medial
	16	M	Right popliteal artery	Aneurysm	Thrombosis	Resection	Good	Medial
Tisnado et al. (1982)	69	F	Bilateral femoral to popliteal arteries	Beaded	Microemboli of toes	Conservative	good	N/A
Iwai et al. (1985)	65	F	Bilateral popliteal arteries	Beaded	Claudication	Angioplasty Sympathectomy	Good	Medial
	25	F	Right popliteal artery	Beaded	None	None	Good	N/A
	48	M	Right deep femoral artery	Beaded	Raynauds syndrome	Sympathectomy	Good	N/A
Stinnet et al. (1987)	10	F	Bilateral popliteal arteries	Aneurysm	Claudication	Bypass	Good	Medial hyperplasia
Dungen et al. (1990)	15	F	Right superficial femoral artery	Occlusion	Claudication	Bypass	Good	Perimedial fibroplasia
	21	M	Left superficial femoral artery	Occlusion	Claudication	Sympathectomy and bypass	Amputation	Medial dissection
	36	M	Left popliteal artery	Occlusion	Claudication	Bypass	Good	Intimal
Fiche et al. (1991)	20	M	Right popliteal artery	Aneurysm	Knee effusion	Interposition	Good	Medial
Neukirch et al. (1996)	39	F	Left popliteal artery	Aneurysm	None	Resection and anastomosis	Good	Media
present case (2009)	63	F	Bilateral femoral to popliteal arteries	Beaded	Claudication	Bypass	Good	Medial

FMD, fibromuscular dysplasia

renal arteries and extrarenal vessels. In 1982, Mettinger and Ericson reviewed reports concerning 1197 patients with FMD.¹² Renal arteries were involved in 58%, cervicocranial arteries in 32%, visceral arteries in 25%, and iliac arteries in 25% of cases. Of these nearly 1200 cases, only one was located in an infrainguinal artery of the lower extremity.

To the best of our knowledge, only 13 cases of FMD of the femoral or popliteal artery have been reported in the literature, including case 1 in the present report (Table 1).¹³⁻¹⁹ Of these 13 cases, seven were female and six were male, the mean age was 33 years, and the age range was 1-69 years. Angiographically, six cases appeared beaded, four were single aneurysms, and three were total occlusions. Eight cases of FMD of the femoral or popliteal artery had histological FMD diagnoses: seven were medial and one intimal.

Although FMD of the iliac artery (the third most common arterial site) with a beaded appearance or with

aneurysm formation has been well documented, iliac artery dissection caused by FMD has been rarely reported. To our knowledge, only 12 cases of iliac artery dissection associated with FMD have been reported, including case 2 in this report (Table 2).²⁰⁻²⁶ Of these cases, seven were male and five were female. The mean age was 42 years, and the age range was 21-56 years. Most patients presented with leg ischemia or local pain, underwent bypass or resection and interposition, and had good outcomes. Two patients involved rupture and hypovolemic shock; and, in both cases, the patients died post-operatively. Seven reported cases of FMD of the iliac artery have had histological diagnoses; all were medial FMD. Although our case was asymptomatic, an operative indication was decided from the progressive enlargement of the dissected pseudolumen, newly developed contralateral iliac dissection, and possible disastrous consequences of ruptured dissecting aneurysm.

It is generally not considered difficult to differentiate

Table 2 Iliac artery dissection associated with FMD

Author (year)	Age	Sex	Site of dissection	Symptom	treatment	Outcome	histology
Burri et al. (1983)	45	F	Left external iliac artery	Inguinal pain	Bypass	Good	medial
Sauer et al. (1990)	56	F	Right common iliac artery	Claudication	Conservative	Good	N/A
Patel et al. (1990)	39	M	Left external iliac artery	Inguinal pain	Bypass	Good	medial
Thevernet et al. (1992)	45	F	Right external iliac artery	Leg ischemia	Bypass	Good	medial
	51	M	Bilateral external iliac arteries	Claudication	Bypass	Good	N/A
	47	F	Right external iliac artery	Abdominal pain	Bypass	Good	N/A
	29	F	Left external iliac artery	Abdominal pain	Interposition with vein	Good	N/A
	53	M	Right external iliac artery	Claudication	Bypass	Good	N/A
Luck et al. (2002)	45	M	Right external iliac artery	Claudication	Endarterectomy	Good	medial
Honjo et al. (2004)	30	M	Left common iliac artery	Shock, rupture	Bypass	Dead	medial
Yoshioka et al. (2005)	21	M	Left common iliac artery	Abdominal pain, rupture	Bypass	Dead	medial
present case (2009)	37	M	Bilateral external iliac arteries	none	Interposition with ePTFE	Good	medial

FMD, fibromuscular dysplasia

atherosclerosis from FMD. Atherosclerosis typically occurs in older patients with typical cardiovascular risk factors. On the other hand, FMD usually occurs in younger patients who have few cardiovascular risk factors. Lacking specific markers or effective non-invasive tests, angiographic imaging is almost essential for the diagnosis of FMD. Recently, computed tomographic angiography or gadolinium-enhanced magnetic resonance angiography have emerged as less invasive diagnostic imaging compared to contrast-enhanced digital subtraction angiography. Although the “string of beads” appearance is well known as a specific angiographic feature of FMD, FMD subtypes other than medial fibroplasia can present with a wide variety of angiographic appearances. For example, intimal fibroplasia and medial hyperplasia may present as a smooth or focal stenosis. Perimedial fibroplasias also may present with “string-of-beads” appearance. However, the beads in perimedial fibroplasia do not exceed the original arterial lumen. Kincaid et al. reported that “string-of beads” appearances were observed in 78 (62%) of 125 patients with renal FMD.²⁷⁾ In cervicocranial vessels, Mettinger et al. reported that 26 (62%) of 37 patients had a “string-of-beads” appearance.²⁸⁾ In cases of infrainguinal femoral and popliteal arteries, 6 (46%) of 13 had a “string-of-beads” appearance (Table 1). Therefore, the “string-of-beads” appearance can be specific to medial fibroplasia, but is not sensitive

enough to diagnose all cases of FMD. Moreover, these angiographic signatures are only visible at the early stage of disease. Once an occluded vessel takes on atherosclerotic and/or inflammatory features, it can be difficult to distinguish FMD from atherosclerosis or arteritis without histological confirmation. The collection of tissue for histological analysis may not be possible from occluded peripheral arteries treated with bypass surgery. Therefore, a fair amount of peripheral arterial occlusion caused by fibrodysplastic disease may be misdiagnosed as a common atherosclerotic disease.

FMD of lower extremities may cause both acute and chronic leg ischemia by luminal stenosis, thrombosis and distal embolism. It may present with cold legs, intermittent claudication, ischemic ulcer or limb gangrene and may require arterial reconstruction.

Treatment of FMD of the extremities includes anticoagulation, lumbar sympathectomy, bypass surgery, aneurysm resection, and interposition, depending upon the arterial segments involved. Recently, successful percutaneous transluminal angioplasty and endovascular therapy have also been reported.²⁹⁻³¹⁾

In conclusion, fibromuscular dysplasia should be considered as a potential cause of arterial occlusion, stenosis, dissection or aneurysm in the peripheral arteries. Although it is a rare cause of such pathologies, FMD may lead to life-threatening hemorrhage or limb-threat-

ening ischemia.

REFERENCES

- 1) Leadbetter WF, Burkland CE. Hypertension in unilateral renal disease. *J Urol* 1938; **39**: 611–5.
- 2) Slovut DP, Olin JW. Fibromuscular dysplasia. *N Engl J Med* 2004; **29**: 1862–71.
- 3) Harrison EG Jr, McCormack LJ. Pathologic classification of renal arterial disease in renovascular hypertension. *Mayo Clin Proc* 1971; **46**: 161–7.
- 4) Insall RL, Chamberlain J, Loose HWC. Fibromuscular dysplasia of visceral arteries. *Eur J Vasc Surg* 1992; **6**: 668–72.
- 5) Sang CN, Whelton PK, Hamper UM, Connolly M, Kadir S, White RI, et al. Etiologic factors in renovascular fibromuscular dysplasia. A case-control study. *Hypertension* 1989; **14**: 427–9.
- 6) Pannier-Moreau I, Grimbert P, Fiquet-Kempf B, Vuagnat A, Jeunemaitre X, Corvol P, et al. Possible familial origin of multifocal renal artery fibromuscular dysplasia. *J Hypertens* 1997; **15**: 1797–801.
- 7) Rushton AR. The genetics of fibromuscular dysplasia. *Arch Intern Med* 1980; **140**: 233–6.
- 8) Perdu J, Boutouyrie P, Bourgain C, Stern N, Laloux B, Bozec E, et al. Inheritance of arterial lesions in renal fibromuscular dysplasia. *J Hum Hypertens* 2007; **21**: 393–400.
- 9) Schievink WI, Limburg M. Angiographic abnormalities mimicking fibromuscular dysplasia in patient with Ehlers-Danlos syndrome, type IV. *Neurosurgery* 1989; **25**: 482–3.
- 10) Schievink WI, Bjornsson J, Piepgras DG. Coexistence of fibromuscular dysplasia and cystic medial necrosis in a patient with Marfan's syndrome and bilateral carotid artery dissections. *Stroke* 1994; **25**: 2492–6.
- 11) Bofinger A, Hawley C, Fisher P, Daunt N, Stowasser M, Gordon R. Polymorphisms of the renin-angiotensin system in patients with multifocal renal arterial fibromuscular dysplasia. *J Hum Hypertens* 2001; **15**: 185–90.
- 12) Mettinger KL. Fibromuscular dysplasia and the brain II. Current concept of the disease. *Stroke* 1982; **13**: 53–8.
- 13) Prince RA, Vawter GF. Arterial fibromuscular dysplasia in infancy and childhood. *Arch Pathol* 1972; **93**: 419–26.
- 14) Tisnado J, Barnes RW, Beachley MC, Vines FS, Amendora MA. Fibrodysplasia of the popliteal arteries. *Angiology* 1982; **33**: 1–5.
- 15) Iwai T, Konno S, Hiejima K, Satake S, Suzuki S, Hiranuma S, et al. Fibromuscular dysplasia in the extremities. *J Cardiovasc Surg* 1985; **26**: 496–501.
- 16) Stinnett DM, Graham JM, Edwards WD. Fibromuscular dysplasia and thrombosed aneurysm of the popliteal artery in a child. *J Vasc Surg* 1987; **5**: 769–2.
- 17) Dungen JJAM, Boontje AH, Oosterhuis JW. Femoropopliteal arterial fibrodysplasia. *Br J Surg* 1990; **77**: 396–9.
- 18) Fiche M, Patra P, Chaillou P. Medial fibrodysplasia and aneurysm of the popliteal artery. *Ann Vasc Surg* 1991; **5**: 456–8.
- 19) Newkirk C, Bahnini A, Delcourt A, Kieffer E. Popliteal aneurysm due to fibromuscular dysplasia. *Ann Vasc Surg* 1996; **10**: 578–81.
- 20) Burri B, Fontollet C, Rueggsegger CH, Mosimann R. External iliac artery dissection due to fibromuscular dysplasia. *VASA* 1983; **12**: 76–8.
- 21) Sauer L, Reilly LM, Goldstone J, Ehrenfeld WK, Hutten JE, Stoney RJ. Clinical spectrum of symptomatic fibromuscular dysplasia. *J Vasc Surg* 1990; **12**: 488–96.
- 22) Patel KS, Wolfe JH, Mathias C. Left external iliac artery dissection and bilateral renal artery aneurysms secondary to fibromuscular dysplasia: a case report. *Neth J Surg* 1990; **42**: 118–20.
- 23) Thevenet A, Latil JL, Albat B. Fibromuscular disease of the external iliac artery. *Ann Vasc Surg* 1992; **6**: 199–204.
- 24) Luck I, Hanschke D, Geibler C, Grub JD. Spontaneous dissection of the external iliac artery due to fibromuscular dysplasia. *VASA* 2002; **31**: 115–21.
- 25) Honjo O, Yamada Y, Kuroko Y, Kushida Y, Une D, Hioki K. Spontaneous dissection and rupture of common iliac artery in a patient with fibromuscular dysplasia: A case report and review of the literature on iliac artery dissections secondary to fibromuscular dysplasia. *J Vasc Surg* 2004; **40**: 1032–6.
- 26) Yoshioka I, Arichi N, Tokugawa S, Kishikawa H, Nishimura K, Ichikawa Y. Spontaneous rupture of common iliac artery associated with fibromuscular dysplasia presenting with colic pain suggestive of ureteral stone. *Acta Urol Jpn* 2007; **53**: 721–4.
- 27) Kincaid OW, Davis DG, Hallermann FJ, Hunt JC. Fibromuscular dysplasia of the renal arteries: arteriographic features, classification, and observation on natural history of the disease. *Am J Roentogenol* 1968; **104**: 271–82.
- 28) Mettinger KL, Ericson K. Fibromuscular dysplasia and the brain: Observation on angiographic, clinical and genetic characteristics. *Stroke* 1982; **13**: 46–52.
- 29) Shin JS, Han EM, Min BZ, Jung WJ, Jo WM, Lee IS. Fibromuscular dysplasia of bilateral brachial arteries with surgery and consecutive thrombolytic therapy. *Ann Vasc Surg* 2007; **21**: 93–6.
- 30) Iida O, Nanto S, Uematsu M, Morozumi T, Akahori H, Nagata S. Endovascular therapy for limb salvage in a case of critical lower limb ischemia resulting from fibromuscular dysplasia. *J Vasc Surg* 2007; **46**: 803–7.
- 31) Yoshida T, Ohashi I, Suzuki S, Iwai T. Fibromuscular disease of the brachial artery with digital emboli treated effectively by transluminal angioplasty. *Cardiovasc Intervent Radiol* 1994; **17**: 99–101.

» **Case Report** «

Surgical Repair of Arteriovenous Fistula Associated with Infrarenal Aorto-iliac Aneurysm: Report of Two Contrasting Cases

Norihiro Kondo, MD, Kenji Takahashi, MD, Susumu Takeuchi, MD, and Kazuo Ito, MD

We present two cases of arteriovenous fistulas associated with aneurysms of the infrarenal aorta or common iliac artery. A definitive diagnosis is sometimes difficult given the varied and unclear presentation. However, with the correct preoperative diagnosis, mortality can be reduced. Both cases, being reported here, were diagnosed preoperatively and underwent alternate surgical repairs. One case was treated by aortic exclusion, whereas the second case was treated by primary closure of the fistula. Repair techniques were chosen based on acuity of presentation. Given our experience with these two cases, we conclude that direct closure is possible but dependent on the chronicity of the lesion.

Key words: arteriovenous fistula, surgical repair, ruptured aorto-iliac aneurysm

INTRODUCTION

Arteriovenous fistula (AVF) of the infrarenal aorta is a well known clinical entity, which left untreated carries a high mortality rate. They can occur secondary to erosion of either an abdominal aortic aneurysm (AAA) or common iliac artery aneurysms (CIAAs) into the adjacent vena cava.¹⁻³⁾ The reported incidence is 0.3%–4.5% of all patients undergoing surgical treatment for aorto-iliac aneurysms¹⁻³⁾ and 6.4%–8.8% among those operated on for ruptured aneurysms.^{1, 2, 4)} Classic teaching describes AVF presenting with the triad of symptoms: congestive heart failure, a continuous abdominal bruit, and a pulsating abdominal mass. However, the clinical presentation can be subtle and varied leading to a lack of a preoperative diagnosis.^{2, 5)} Consequently, massive bleeding can ensue intra-operatively. Therefore, an astute preoperative diagnosis can help in identifying optimal operative ap-

proaches and minimize intra-op blood loss. We present two cases of AVFs in which the lesion had been diagnosed preoperatively and each patient underwent a tailored repair technique.

CASE REPORT

Case 1

A 55-year-old man presented to our emergency room complaining of low abdominal pain, right leg pain, and anuria for 12 hours. Physical examination demonstrated a soft, non-distended, nontender abdomen without palpable masses or bruits. His legs were non cyanotic. Of note, the patient was 167 cm tall and weighed 87 kg making deep palpation of the abdomen difficult. Urethral catheterization obtained 20 mL of gross hematuria. Non contrast abdominal and pelvic computed tomography (CT) showed an infrarenal AAA with bilateral CIAAs. Enhanced CT revealed a right common iliac artery aneurysm measuring 6 cm in diameter, which was abutting and possibly involving the common iliac vein. The aneurysmal wall was thin and the right iliac vein enhanced in the arterial phase (**Fig. 1**). The patient was hemodynamically stable with a normal chest X-ray. Nevertheless, an urgent operation was performed with a provisional diagnosis of AVF to a ruptured iliac artery aneurysm. Surgical

Aomori City Hospital, Department of Cardiovascular Surgery, Aomori, Aomori, Japan

Received: August 2, 2010; Accepted: March 9, 2011
Corresponding author: Norihiro Kondo, MD, Aomori City Hospital, Department of Cardiovascular Surgery, 1-14-20 Katta, Aomori, Aomori 031-0821, Japan
Tel: +81-17-734-2171, Fax: +81-17-734-7578
E-mail: kondo18@r66.7-dj.com



Fig. 1 Preoperative abdominal computed tomography image from Case 1 demonstrates an aneurysm of the right common iliac artery with thinning of the aneurysmal wall. The right iliac vein was enhanced in the arterial phase.

approach was a median laparotomy. After standard proximal and distal control, the aneurysm was opened. At this point, a large amount of venous blood pooled into the operative field from an AVF, measuring 3.0 cm × 1.0 cm, originating distal to the aortic bifurcation. Direct closure was attempted, however, the fistula wall was extremely fragile, similar in consistency to necrotic tissue. Given the lack of tissue integrity to support a surgical repair it was decided to close the aneurysmal wall and manage the AVF with an aortic exclusion procedure.⁶⁾ The lumbar arteries were oversewn, and the aneurysm sac was closed. AVF bleeding was controlled by venous compression. The aneurysm sac was excluded by ligation and oversewing proximally and distally (**Fig. 2**). An anatomical reconstruction was performed with a 20-mm woven Dacron bifurcated graft (**Fig. 2**). His hematuria resolved almost immediately. However, the patient had a prolonged post operative course (53 days) complicated by a non mechanical intestinal obstruction, and he had no direct procedure-related complications. He did not require hemodialysis and no evidence was found to suggest deep vein thrombosis or pulmonary thromboembolism.

Case 2

A 66 year old man was referred to the Department of

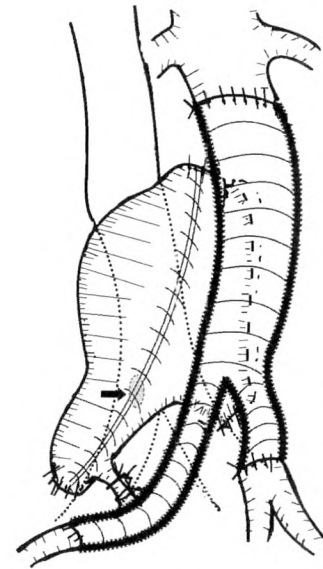


Fig. 2 Schematic illustration of the surgical repair used in Case 1. The aorta was divided proximally and the aneurysmal wall was oversewn proximal to its distal aortotomy edge. A Y-shaped graft was anastomosed in an end-to-end fashion. The position of the fistula (solid arrow) is shown behind the right common iliac aneurysm.

Cardiology at our institution for evaluation of a systolic abdominal bruit. He had no symptoms, but chest X-ray showed a right sided pleural effusion. Contrast enhanced CT showed an infrarenal AAA measuring 8.3 cm × 7.0 cm. The lesion was compressing the adjacent IVC, and there appeared to be contrast leakage into the inferior vena cava (**Fig. 3**). The patient was immediately transferred to our service and taken to the operating room for an emergent repair of the aneurysm. Our approach was a median laparotomy. The AAA was identified and proximal, and distal control was obtained. The aneurysmal sac was opened, the adherent thrombus was removed, and venous blood was noted to be pooling into the field. A 2 cm × 1 cm communication was identified between the aneurysmal wall and the vena cava. Venous bleeding was controlled by direct compression. The wall of the AVF was solid, thereby permitting direct closure with felt strip reinforcements. The patient had an uneventful post operative course and was discharged after 21 days.

DISCUSSION

The overall incidence of AVFs is cited as 0.2% to 2.2% of all infrarenal aortoiliac aneurysms undergoing surgery.¹⁻³⁾ Aneurysmal erosion into the venous system is the most common etiology for communication between the

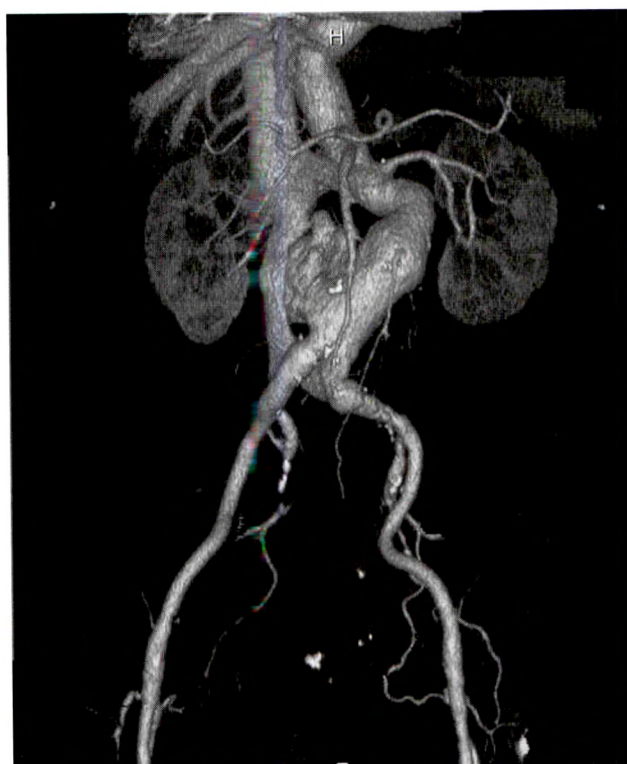


Fig. 3 Preoperative abdominal computed tomography from Case 2 revealed the contrast media leaking into the inferior vena cava, which was compressed and involved with the aneurysm.

two systems.¹⁻³⁾ The erosion results from spontaneous rupture of an atherosclerotic aneurysm directly into the adjacent vein. The current theory behind the development of these fistulas is that pressure and tension from large aneurysms produce necrosis of the aortic wall. This results in an adventitial inflammatory reaction and recruitment of adjacent vein(s) to the diseased artery. The inflammation progresses until the arterial wall ruptures into the venous system, creating a fistula.⁴⁾

Diagnosing an AVF can be difficult because the classic signs (pulsatile abdominal mass with bruit and high-output heart failure) are present in only 20%–50% of reported cases.⁵⁾ Patients with AVF present atypically¹⁾ with decompensated congestive heart failure occurring in only 35% of cases.⁵⁾ As an example, our second patient had a chest X-ray with a right sided pleural effusion but was otherwise asymptomatic. Takazawa et al. reported the following as reasons for a delay in diagnosis: 1) shock often obscures symptoms when an immediate operation is needed 2) there is decreased shunt flow due to venous compression by large aneurysms 3) there is often time partial obstruction of the AVF by mural thrombus.⁵⁾ Such

compression can compromise venous return to the heart and elevate peripheral venous pressures. This can manifest as swelling of the lower extremities,²⁾ hematuria,⁷⁾ renal insufficiency,^{2, 7)} scrotal edema, and even rectal bleeding.¹⁾ If attention is directed purely on these secondary symptoms, there will inherently be a delay in diagnosing and treating AVFs. This delay can be catastrophic given a mortality rate of 30%.⁶⁾ The condition thus requires a prudent preoperative diagnosis and urgent repair. The quoted operative mortality rate of AVF repairs ranges from 16%–66%.¹⁻³⁾ This relatively high mortality rate is attributed to other co-morbidities as age, coronary artery disease and congestive heart failure.

Having the correct preoperative diagnosis can reduce intraoperative blood loss when performing an urgent AVF repair. Nevertheless, control of venous bleeding remains a challenge. Manual compression proximally and distally to the fistula is a useful maneuver.¹⁾ Alternatively, balloon occlusion via a transfemoral or transfistular insertion can be attempted. In the event of irretractable venous bleeding from the AVF, it may be necessary to ligate the IVC.^{1, 3)} The ideal approach to control

bleeding would be to snare the proximal IVC and the distal portion of the AVF. However, this can be difficult given the adhesions between the arteries and the vein. This approach was attempted but abandoned in the present two cases considering the possibility of venous injury.

In the event of a friable wall, direct closure can be difficult. The exclusion method⁶⁾ can be useful as it avoids manipulating the fragile fistula.

A potential complication of this method is deep vein thrombosis (DVT) as reported by Wooley and colleagues.⁶⁾ A relationship might exist between venous thrombus and the thrombus in the excluded aortic segment.⁶⁾ In our first case, the aneurysmal sac was filled with thrombus. However, the thrombus remained stable not to be dislodged from the cavity into the venous system. The clot would eventually become organized, and the venous opening would be closed with scar tissue.⁴⁾ Venous thrombosis remains a reported complication after surgery for ruptured aortic aneurysms.⁸⁾ Since DVTs can be multi-factorial, it is crucial to keep the venous system intact and implement standard DVT precautions. The possibility of direct closure might depend on the chronicity of the fistula. The present cases illustrate that closure should be avoided in the acute scenario (e.g., Case 1), while entertained in the chronic scenario (e.g., Case 2).

Because of its rarity and associated technical difficulties, AVFs presents a challenge to the vascular surgeon. However with an early preoperative diagnosis, minimization of blood loss and use of appropriate bypass techniques, satisfactory outcomes can be attained.

ACKNOWLEDGEMENTS

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REFERENCES

- 1) Cinara IS, Davidovic LB, Kostic DM, Cvetkovic SD, Jakovljevic NS, Koncar IB. Aorto-caval fistulas: a review of eighteen years experience. *Acta Chir Belg* 2005; **105**: 616–20.
- 2) Huang Y, Gloviczki P, Duncan AA, Kalra M, Hoskin TL, Oderich GS, et al. Common iliac artery aneurysm: expansion rate and results of open surgical and endovascular repair. *J Vasc Surg* 2008; **47**: 1203–10.
- 3) Davis PM, Gloviczki P, Cherry KJ Jr, Toomey BJ, Stanson AW, Bower TC, et al. Aorto-caval and ilio-iliac arteriovenous fistulae. *Am J Surg* 1998; **176**: 115–8.
- 4) Uemura Y, Okagawa K, Kawasaki T, Monden M, Kambayashi J, Morimoto F, et al. A unique method of closure for an aortocaval fistula in association with a ruptured abdominal aortic aneurysm: report of a case. *Surg Today* 1998; **28**: 1213–6.
- 5) Takazawa A, Sakahashi H, Toyama A. Surgical repair of a concealed aortocaval fistula associated with an abdominal aortic aneurysm: report of two cases. *Surg Today* 2001; **31**: 842–4.
- 6) Woolley DS, Spence RK. Aortocaval fistula treated by aortic exclusion. *J Vasc Surg* 1995; **22**: 639–42.
- 7) Brunkwall J, Lanne T, Bergentz SE. Acute renal impairment due to a primary aortocaval fistula is normalised after a successful operation. *Eur J Vasc Endovasc Surg* 1999; **17**: 191–6.
- 8) Kondo N, Koyama M, Minakawa M, Ito K, Ono Y, Fukui K, et al. A case of inferior vena caval thrombosis obstruction for a ruptured abdominal aortic aneurysm. *Jpn J Phlebology* 2002; **13**: 55–60. (in Japanese)

► Case Report ◀

Pseudoaneurysm in the Left Groin due to Ruptured Knitted Dacron Graft

Masahiro Ryugo, MD, Takumi Yasugi, MD, Mitsugi Nagashima, MD, Hironori Izutani, MD, Toru Okamura, MD, Fumiaki Shikata, MD, Masashi Kawamura, MD, and Kanji Kawachi, MD

An 82-year-old man was admitted to our institution with a painful pulsating mass in the left groin. He had undergone bypass surgery with a bifurcated Cooley double velour knitted Dacron graft to treat aorto-iliac occlusive disease 21 years previously. Computed tomography demonstrated a 35-mm pseudoaneurysm near the distal anastomosis site of the graft. Opening the aneurysm revealed that the graft was disrupted along the guideline. We resected the aneurysm and interposed an expanded polytetrafluoroethylene (ePTFE) graft. Vascular surgeons should consider that grafts can fail in patients with long-term prosthetic grafts.

Key words: endovascular aortic repair, polyester vascular prostheses, degradation

CASE REPORT

An 82-year-old man with claudication due to aortoiliac occlusive disease in both legs was treated in 1988 at another hospital by an aorto-bifemoral bypass using a bifurcated Cooley double velour knitted Dacron (CD-VKD) graft. He was admitted to our institution in 2007 with a pseudoaneurysm of the proximal anastomotic site, and treated by endovascular aortic repair using a hand-made stent graft via an approach from the right limb of the bifurcated graft (**Fig. 1a**).

He was admitted to our institution again in January 2010 with a painful pulsating mass in the left groin. The left dorsal pedal and posterior tibial arteries were palpable and the thigh was slightly swollen due to compression of the femoral vein by the mass. Computed tomography (CT) indicated a 35-mm para-anastomotic pseudoaneurysm of the left limb of the graft that was not detected in 2007 (**Fig. 1b**). The graft was replaced to avoid rupture

of this aneurysm.

The operation proceeded under general anesthesia with the patient in the supine position. The proximal site of the aneurysm of the previous bypass graft just above the inguinal ligament, as well as the superficial and deep femoral arteries, were encircled and clamped. Opening the aneurysmal wall and removing some thrombus revealed a Dacron graft that had become disrupted along the guideline (**Fig. 2**). No changes were evident at the previous anastomotic portion. The area from the intact part of the Dacron graft to the native superficial femoral artery was replaced with an 8-mm-ringed expanded polytetrafluoroethylene (ePTFE) graft, and we reconstructed the deep femoral artery using an interposed 8-mm ringed ePTFE graft.

A postoperative CT scan did not confirm an inappropriate blood flow in the operative area and also showed a patent reconstructed ePTFE graft. Microscopic examination of the resected specimen revealed a relatively loose array of fibers, a few seeds of intimal cells and inflammatory cell infiltration at the site of the guideline, indicating that the Dacron graft had deteriorated (**Fig. 3**). The postoperative course of the patient was uneventful except for prolonged wound healing due to chronic perianeurysmal inflammatory changes, and he was discharged two months after the operation.

Department of Cardiovascular Surgery, Ehime University Hospital, To-on, Ehime, Japan

Received: December 14, 2010; Accepted: March 14, 2011
Corresponding author: Masahiro Ryugo, MD. Department of Cardiovascular Surgery, Ehime University Hospital, Shitsukawa, To-on, Ehime 791-0295, Japan
Tel: +81-089-960-5331, Fax: +81-089-960-5335
E-mail: ryugou@m.ehime-u.ac.jp

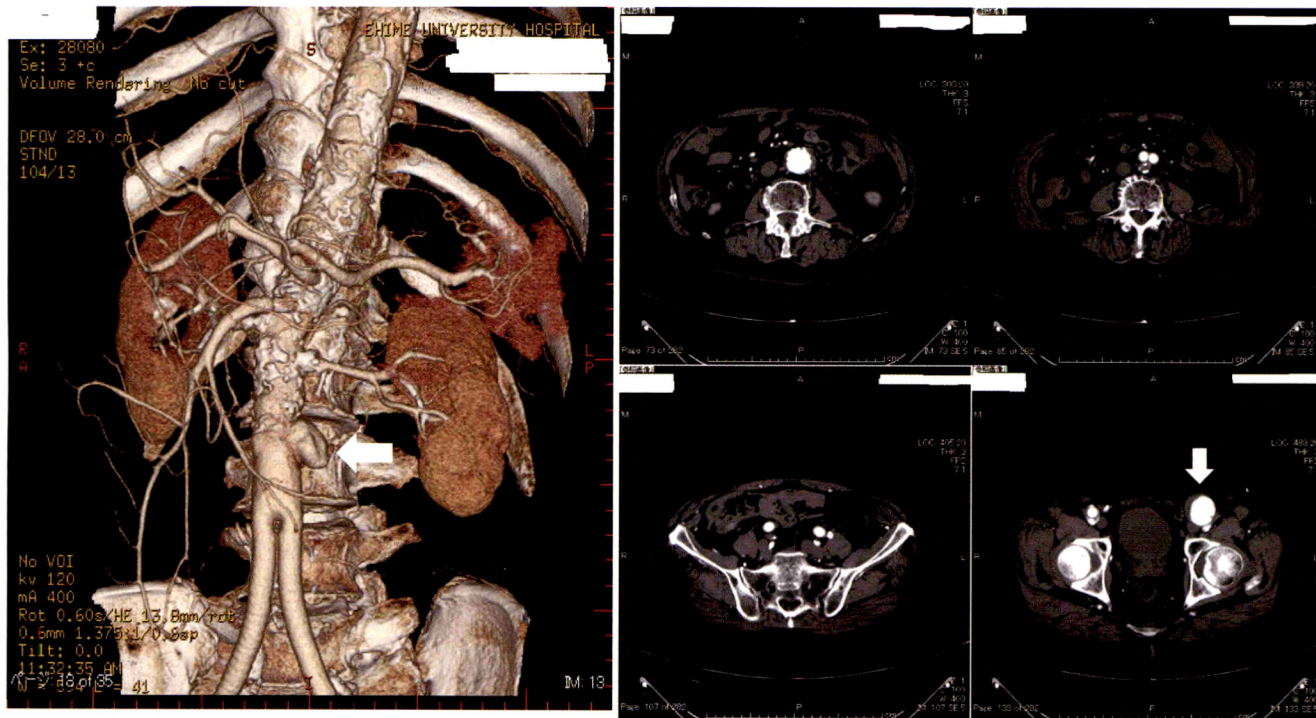


Fig. 1 Computed tomography findings.

Three-dimensional CT scan of para-anastomotic pseudoaneurysm of proximal anastomotic site (arrow) in 2007 (A). CT scan in 2010 (B) shows 35-mm pseudoaneurysm in left groin, 2 cm above end-to-side anastomotic portion of previous bifurcated graft bypass.

CT, computed tomography

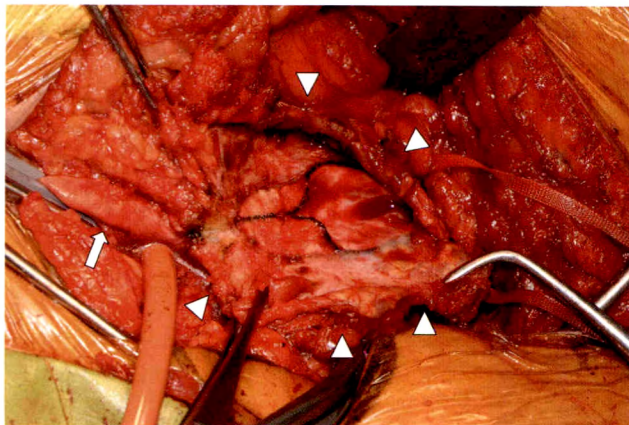


Fig. 2 Intraoperative photograph shows disrupted left graft limb beneath guideline.

Arrow, left superficial femoral artery; arrowheads, opened wall of pseudoaneurysm

DISCUSSION

We described the rare rupture of a knitted Dacron graft after 21 years in situ. The presence of a few graft fibers in the aneurysmal site upon microscopic examination indicated that rupture might have followed graft

dilation. In addition, the pseudoaneurysm of the proximal anastomotic site that was treated by endovascular repair in 2007 might also have caused the graft to deteriorate.

Several reports have described aneurysms or late-stage disruption of CDVKD grafts.^{1–4} Most of them focus on aneurysmal changes or rupture of CDVKD grafts produced before 1982. Despite the assertion by Meadox Medical Inc. that aneurysmal changes have not occurred since the second-generation product was introduced in 1982, some reports have indicated otherwise.^{5–6}

Intrinsic Dacron grafts fail in 0.5%–3% of patients. The average duration between implantation and the detection of graft failure is 77 months.⁷ Long term degradation is a complication of polyester vascular prostheses, including knitted Dacron grafts, that might lead to dilation or prosthetic rupture.^{8–9} Degradation might be related to several factors, such as the structural nature of the textile, changes in the prosthesis during the manufacturing process or during implantation by handling or clamping. Secondary physicochemical alterations when the prosthesis is exposed to a chronic inflammatory reaction to foreign bodies and systolo-diastolic arterial stress might also contribute to degradation.¹⁰ Aneurysms in the

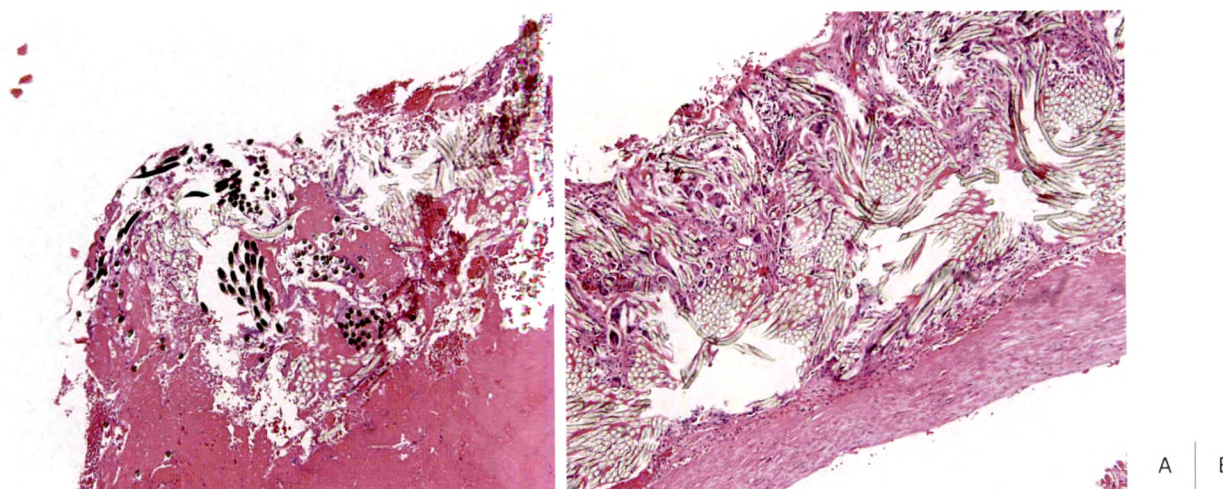


Fig. 3 Microscopic findings of site of graft disruption.

Guideline site (A) and site opposite guideline (B). Dyed yarn (black) indicate guideline site. Fibers are relatively loose and inflammatory cells have infiltrated around Dacron graft at guideline site, indicating deterioration.

groin are usually located in aorto-iliac or aorto-femoral bypass grafts, followed by the costal arch in axillo-femoral bypass grafts. These findings indicate the influence of medical stress on the grafts. Chakfe et al. analyzed the textile structure of 20 knitted polyester vascular prostheses, including 15 CDVKD grafts, and found that longitudinal ruptures always occur in two specific areas of the prosthesis, namely at the guideline and at the remeshing line.¹¹⁾ The guideline is produced by incorporating a dyed yarn in the knit, and its function is to avoid the prosthesis twisting at the time of implantation. The remeshing line is created by a knit technique. These two lines might represent areas of weakness in such prostheses. The graft ruptured at the guideline in our patient.

Patients implanted with Dacron grafts require regular and long term follow-up by CT scanning and physical examinations to avoid late-stage graft disruption and fatal hemorrhage. All dilated portions should be surgically removed, and replacement with an ePTFE graft might be advisable as in the present case, because late stage rupture of these grafts is rare.

We described a rare late stage rupture of a bifurcated knitted Dacron graft. We surgically reconstructed the previous graft using new ringed ePTFE grafts. The remainder of the previous graft is under strict follow up.

REFERENCES

- 1) Magee HR, Teague CA. Late rupture of knitted velour Dacron arterial prostheses. *Aust N Z J Surg* 1988; **58**: 549–53.
- 2) Blumenberg RM, Gelfand ML. Failure of knitted Dacron as an arterial prosthesis. *Surgery* 1977; **81**: 493–6.
- 3) Nakajima J, Ikegami T, Ishihara T, Murakami K, Morimoto K. A false aneurysm caused by rupture of a double velour Dacron graft. A case report. *Nippon Geka Gakkai Zasshi* 1986; **87**: 921–5. (in Japanese)
- 4) Kawamura M, Ogino H, Matsuda H, Minatoya K, Sasaki H, Kitamura S. Late-Stage, nonanastomotic rupture of double velour Dacron graft after descending aortic replacement. *J Thorac Cardiovasc Surg* 2006; **132**: 961–2.
- 5) Hatayama M, Ono Y, Itaya H. False aneurysm in the right groin due to disruption of a knitted Dacron prosthesis. *Jpn J Cardiovasc Surg* 2009; **38**: 372–5. (in Japanese)
- 6) Ogata K, Shindou S, Kojima A, Kobayashi M, Katahira S, Katsu M, et al. False aneurysm in the right groin due to disruption of a knitted Dacron graft. *Jpn J Cardiovasc Surg* 2003; **32**: 280–4. (in Japanese)
- 7) Nunn DB, Pourdeyhimi B. Intrinsic Dacron graft failure 19 years post-implantation. *Cardiovasc Surg* 1997; **5**: 333–8.
- 8) Berger K, Sauvage LR. Late fiber deterioration in Dacron arterial grafts. *Ann Surg* 1981; **193**: 477–91.
- 9) Nunn DB, Freeman MH, Hudgins PC. Postoperative alterations in size of Dacron aortic grafts: an ultrasonic evaluation. *Ann Surg* 1979; **189**: 741–5.
- 10) Pourdeyhimi B, Wagner D. On the correlation between the failure of vascular grafts and their structural and material properties: a critical analysis. *J Biomed Mater Res* 1986; **20**: 375–409.
- 11) Chakfe N, Riepe G, Dieval F, Le Magnen JF, Wang L, Urban E, et al. Longitudinal ruptures of polyester knitted vascular prostheses. *J Vasc Surg* 2001; **33**: 1015–21.

Case Report

Surgical Outcome of Two Difficult Cases with Predominant Proximal Pulmonary Artery Lesions of Chronic Thromboembolic Pulmonary Hypertension

Takashi Murashita, MD, Hitoshi Ogino, MD, PhD, Hitoshi Matsuda, MD, PhD, Hiroaki Sasaki, MD, PhD, Hiroshi Tanaka, MD, PhD, Yutaka Iba, MD, Keitaro Doumae, MD, Tatsuki Fujiwara, MD, Masatoshi Shimada, MD, and Naoki Okuda, MD

Pulmonary endarterectomy (PEA) for chronic thromboembolic pulmonary hypertension (CTEPH) is still challenging. The outcome of patients with proximal pulmonary artery disease is generally better than that of a distal lesion. However, we experienced poor results in two difficult cases having predominant proximal lesions even after effective PEA. Both of them had a long-time history of CTEPH and preoperative condition was critical. Although relatively large amount of thickened intima with massive thrombi were extracted from the proximal pulmonary arteries, they required postoperative percutaneous cardiopulmonary support due to residual pulmonary hypertension. Both of them finally died from pulmonary bleeding and adult respiratory distress syndrome.

Key words: chronic thromboembolic pulmonary hypertension, pulmonary endarterectomy, proximal lesion, distal lesion

INTRODUCTION

Since the San Diego group established surgical procedures for chronic thromboembolic pulmonary hypertension (CTEPH),¹⁻³⁾ successful results of pulmonary endarterectomy (PEA) have been reported from other institutions. However, PEA is still challenging and technically demanding with higher mortality than usual cardiac surgeries. In particular, for patients with distal pulmonary artery disease, PEA is, technically, more difficult and, obviously, its outcome is much poorer than that of proximal disease.⁴⁻⁷⁾ In our previous study, we also reported that the mortality of proximal and distal disease after

PEA was 3.9% and 13.5%, respectively.⁷⁾ In this report, we present two exceptionally difficult cases of severe CTEPH with proximal lesions who died from residual pulmonary hypertension after effective likelihood PEA.

CASE 1

A 40-year-old female with 10 years history of CTEPH who had a deficiency of protein S and C was referred to our hospital for PEA. Since the onset of acute pulmonary embolism ten years ago, dyspnea on effort had gradually progressed. She started home oxygen therapy (HOT) 6 years ago. On admission, she could not walk at all and was always bed-ridden. Her New York Heart Association (NYHA) class was IV. She was on dobutamine of 2 µg/kg/min and intravenous prostacyclin therapy with epoprostenol sodium of 4.5 ng/kg/min. Her oxygen saturation on pulse oximetry was 82% even under HOT. The cardiac catheter study showed that the mean pulmonary artery pressure (mPAP) was 59 mmHg and pulmonary vascular resistance (PVR) was 1855 dynes·sec⁻¹·cm⁻⁵. The cardiac output and cardiac index were 2.4 L/min and 1.7

Department of Cardiovascular Surgery, National Cerebral and Cardiovascular Surgery, Suita, Osaka, Japan

Received: January 4, 2011; Accepted: March 15, 2011
Corresponding author: Hitoshi Ogino, MD. Department of Cardiovascular Surgery, National Cerebral and Cardiovascular Surgery, 5-7-1 Fujishirodai, Suita, Osaka 565-8565 Japan
Tel: +81-6-6833-5012, Fax: +81-6-6833-9865
E-mail: hogino@hsp.ncvc.go.jp

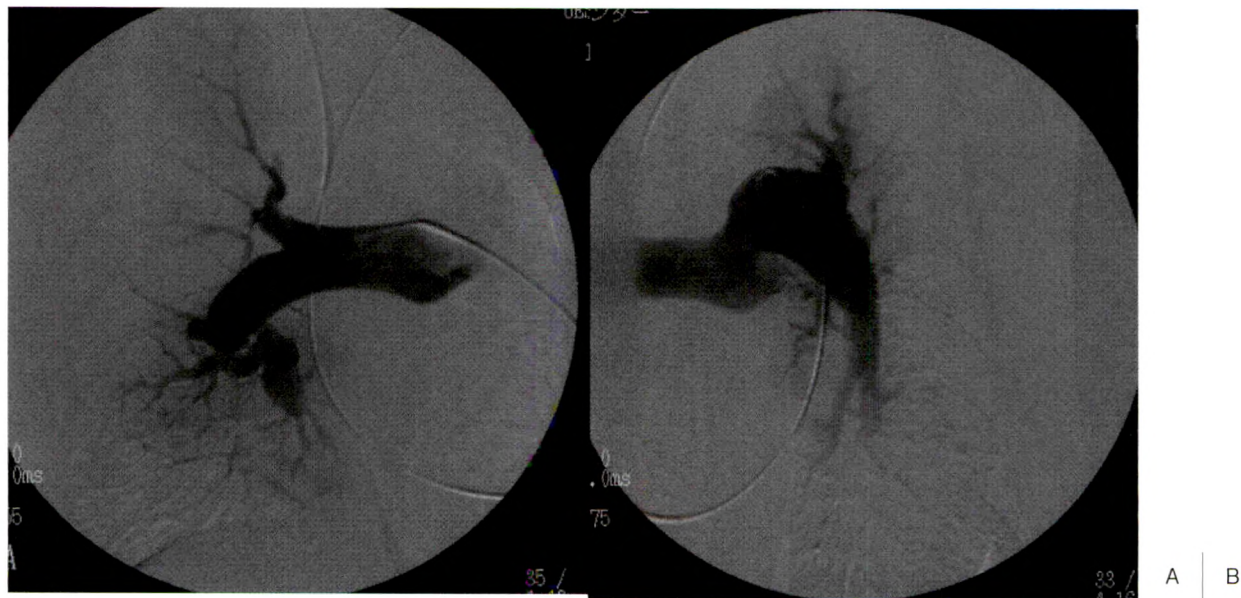


Fig. 1 Preoperative pulmonary artery angiography in case 1. Massive thrombi in the main region and diffuse thrombi in the distal region of both pulmonary arteries.

A: Right pulmonary artery, B: Left pulmonary artery

L/min/m². Pulmonary artery angiography (PAG) shows large thrombi in the both main pulmonary arteries and segmental artery lesions to be accessible at PEA (**Fig. 1**). Transthoracic echocardiography showed severe tricuspid regurgitation and patent foramen ovale (PFO). Brain natriuretic peptide (BNP) level was 1111 ng/ml.

We performed PEA using intermittent deep hypothermia circulatory arrest (DHCA) at 18°C.¹⁻³⁾ Initially, atheromatous change of old thrombi in the both main pulmonary arteries was found. A large amount of thickened intima with them was extracted from the both proximal pulmonary arteries, although PEA was not smoothly done for the distal lesions (**Fig. 3A**). The total circulatory arrest time was 50 minutes. Tricuspid annuloplasty using a 30 mm Edwards MC³ ring and direct closure of PFO were concomitantly performed. Despite PEA, residual pulmonary hypertension developed with mPAP of 60 mmHg. Weaning from cardiopulmonary bypass (CPB) was unsuccessful and percutaneous cardiopulmonary support (PCPS) was used via a femoro-femoral veno-arterial circuit. The patient was transferred to the intensive care unit. The postoperative systemic blood pressure was 100/60 mmHg, PVR was 1538 dynes·cm⁻⁵, and cardiac output was 2.0 L/min. Weaning from PCPS was attempted several times on the following days, but it failed due to residual pulmonary hypertension and right heart failure. On postoperative day (POD) 6, massive pulmonary bleeding from the bronchial artery sud-

denly occurred with support of PCPS and use of heparin. Emergency coil embolization of one branch of the right internal thoracic artery was carried out, and hemostasis was achieved. After that, the condition got stabilized and she was weaned from PCPS on POD 12. However, spontaneous pneumothorax caused deterioration of the respiratory condition with pulmonary hypertension, and PCPS was required on POD 14. In addition, massive pulmonary bleeding occurred again on POD 19, and emergency coil embolization of collateral arteries via the right subclavian artery was performed. Her condition gradually worsened due to pneumonia and acute respiratory distress syndrome (ARDS). Finally, she died from respiratory failure and multiple organ failure on POD 45. The autopsy showed severe pneumonia and bleeding, which made it difficult to identify distal pulmonary lesions.

CASE 2

A 65-year-old male with an 11-year history of CTEPH was referred to our hospital for PEA. Eleven years ago, he also suffered from acute pulmonary embolism and was treated medically. HOT was started at that time. Since then, dyspnea on effort has gradually progressed. On admission, his NYHA class was IV. He was also on dobutamine, 2 µg/kg/min. Deep venous thrombosis (DVT) was detected by ultrasound examination. The cardiac catheter study showed that preoperative mPAP was

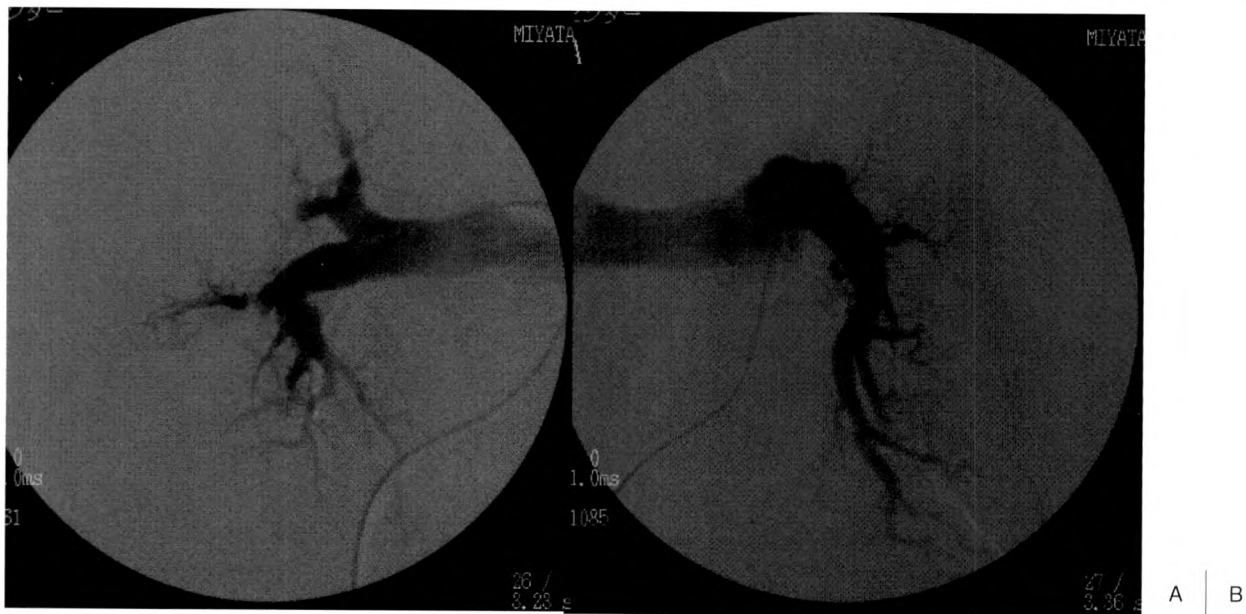


Fig. 2 Preoperative pulmonary artery angiography in case 2. Large thrombi in the right main pulmonary artery and diffuse thrombi in the left pulmonary artery.

A: Right pulmonary artery, B: Left pulmonary artery



Fig. 3 Thickened endothelium with old thrombi extracted from pulmonary arteries in case 1 (A), case 2 (B).

76 mmHg, and PVR was $2,593 \text{ dynes} \cdot \text{sec}^{-1} \cdot \text{cm}^{-5}$. The cardiac output and cardiac index were 2.2 L/min and 1.4 L/min/m^2 . The PAG showed a large thrombi in the right main pulmonary artery and diffuse thrombi in the left pulmonary artery (**Fig. 2**). Transthoracic echocardiography revealed mild to moderate tricuspid regurgitation. Coronary angiography revealed 75% stenosis of the left anterior descending artery (LAD). The BNP level was 1840 ng/ml.

PEA using intermittent DHCA at 18°C with concomitant coronary artery bypass grafting to LAD using saphenous vein graft was carried out. A large amount of thickened intima with old thrombi was extracted from the both sides of pulmonary arteries, predominantly from the proximal pulmonary arteries (**Fig. 3B**). The

total circulatory arrest time was 31 minutes. Weaning from CPB was successful, and he was transferred to the intensive care unit without an assisted device. The post-operative systemic blood pressure was 120/80 mmHg, mPAP was 45 mmHg, PVR was $1347 \text{ dynes} \cdot \text{sec}^{-1} \cdot \text{cm}^{-5}$, and cardiac output was 1.9 L/min.

On POD 2, he was extubated. However, severe reperfusion lung damage occurred on POD 3, and re-intubation was required. On POD 6, PCPS via a femoro-femoral veno-arterial circuit was needed due to deterioration of the hemodynamic state with pulmonary hypertension and severe hypoxia. Chest XP showed findings of ARDS. Steroid pulse therapy was carried out, and his general condition was temporarily improved. He was weaned from PCPS once on POD 9; however, pulmonary bleeding

and pneumonia occurred. ARDS had gradually worsened. Finally, he died from ARDS, pulmonary bleeding, and pneumonia on POD 29. The autopsy showed both sides of pulmonary bleeding and severe pyrothorax.

DISCUSSION

We have reported a relatively low mortality and favorable prognosis with long-term survival after PEA.⁷⁾ The outcome is better in patients with proximal pulmonary artery lesions, although that of patients with distal disease is, in contrast, poorer.⁴⁻⁶⁾ In addition, a previous study showed that patients with a PVR greater than 1.100 dynes·sec⁻¹·cm⁻⁵ and an mPAP greater than 50 mmHg had a poor outcome.⁸⁾ Jamieson et al also reported that 17 of 22 hospital deaths (77%) were related to residual pulmonary hypertension, and the mortality rate was 31% when the postoperative PVR was >500 dynes·sec⁻¹·cm⁻⁵, and 0.9% when it was <500 dynes·sec⁻¹·cm⁻⁵.⁶⁾ In our cases, both had high mPAP and PVR preoperatively, and it did not improve significantly, even after PEA. The postoperative mPAP was 60 mmHg in case 1 and 45 mmHg in case 2, and the postoperative PVR was 1538 dynes·sec⁻¹·cm⁻⁵ in case 1 and 1347 dynes·sec⁻¹·cm⁻⁵ in case 2. Management of residual pulmonary hypertension is still difficult and depends on the severity of pulmonary hypertension, because PVR is commonly fixed and usually does not respond to vasodilators.⁹⁾ Sato et al reported two cases of CTEPH in which they successfully prevented postoperative pulmonary hypertension and hypoxia caused by severe reperfusion pulmonary edema by the use of a percutaneous cardiopulmonary support (PCPS).¹⁰⁾ In our series, 15 patients (11.5%) of 130 patients between 1995 and 2009 including the two presented cases required PCPS for residual pulmonary hypertension with/without pulmonary bleeding. Recently, 8 patients (53.3%) were weaned from it, and 5 (33.3%) of them survived successfully, although the two patients who presented eventually died.

In our cases, both of the patients had a long history of CTEPH more than 10 years and were critically ill with NYHA class IV. Preoperative PVR and mPAP were significantly high. PEA seemed to have a likelihood of success with removal of a large amount of thickened intima; however pulmonary hypertension remains postoperatively. It was speculated that the cause was coexisting distal lesions that had developed in the long-term severe pulmonary hypertension due to a remodeling mechanism. In addition, pulmonary bleeding, unfortunately,

occurred from the lesions of the pulmonary infarction having large collateral arteries in such severe cases having a long history of CTEPH.

In conclusion, some caution is still required in PEA for cases even with proximal type CTEPH having a long history and severe pulmonary hypertension with NYHA class IV.

REFERENCES

- 1) Daily PO, Dembitsky WP, Iversen S, Moser KM, Auger W. Surgical management of chronic pulmonary embolism: surgical treatment and late results. *J Thorac Cardiovasc Surg* 1980; **79**: 523-31.
- 2) Moser KM, Daily PO, Peterson K, Dembitsky W, Vapnek JM, Shure, et al. Thromboendarterectomy for chronic, major-vessel thromboembolic pulmonary hypertension: immediate and long-term results in 42 patients. *Ann Intern Med* 1987; **107**: 560-5.
- 3) Moser KM, Auger WR, Fedullo PF, Jamieson SW. Chronic thromboembolic pulmonary hypertension: clinical picture and surgical treatment. *Eur Respir J* 1992; **5**: 334-42.
- 4) Thistlethwaite PA, Mo M, Madani MM, Deutsch R, Blanchard D, Kapelanski DP, et al. Operative classification of thromboembolic disease determines outcome after pulmonary endarterectomy. *J Thorac Cardiovasc Surg* 2002; **124**: 1203-11.
- 5) Jamieson SW, Auger WR, Fedullo PF, Channick RN, Kriett JM, Tarazi RY, et al. Experience and results with 150 pulmonary thromboendarterectomy operations over a 29-month period. *J Thorac Cardiovasc Surg* 1993; **106**: 116-27.
- 6) Jamieson SW, Kapelanski DP, Sakakibara N, Manecke GR, Thistlethwaite PA, Kerr KM, et al. Pulmonary endarterectomy: experience and lessons learned in 1,500 cases. *Ann Thorac Surg* 2003; **76**: 1457-64.
- 7) Ogino H, Ando M, Matsuda H, Minatoya K, Sasaki H, Nakanishi N, et al. Japanese single-center experience of surgery for chronic thromboembolic pulmonary hypertension. *Ann Thorac Surg* 2006; **82**: 630-6.
- 8) Hartz RS, Byrne JG, Levitsky S, Park J, Rich S. Predictors of mortality in pulmonary thromboendarterectomy. *Ann Thorac Surg* 1996; **62**: 1255-60.
- 9) Reesink HJ, van der Plas MN, Verhey NE, van Steenwijk RP, Kloek JJ, Bresser P. Six-minute walk distance as parameter of functional outcome after pulmonary endarterectomy for chronic thromboembolic pulmonary hypertension. *J Thorac Cardiovasc Surg* 2007; **133**: 510-6.
- 10) Sato M, Ando M, Muto A, Kondo Y, Hoshino R, Nishibe T, et al. Two cases of chronic pulmonary thromboembolism saved by postoperative use of a percutaneous cardiopulmonary support device. *Ann Thorac Surg* 2006; **82**: 314-6.

Case Report

Transient Thrombocytosis after Endovenous Laser Treatment for Primary Varicose Vein of the Lower Extremity

Hiromitsu Sugawara, MD, Masataka Ichiki, MD, Keiijo Sai, MD, Keisuke Kamata, MD, and Makoto Ansai, MD

We presented a case of a completely occluded great saphenous vein and transient thrombocytosis following endovenous laser treatment (EVLT) for primary varicose veins of the lower extremity. A 54-year-old man with a left saphenous varicose vein underwent EVLT surgery. Twelve-watt laser irradiation was delivered over the length of 33 cm of the saphenous vein. The cumulative exposure was 1042 J. Nine days after treatment, the platelet count increased up to $610 \times 10^3/\text{mm}^3$ and returned to normal after 2 months. A complete occlusion of the great saphenous vein commonly occurs after EVLT, but no case of transient thrombocytosis has been reported.

Key words: endovenous laser treatment, thrombocytosis, varicose vein

INTRODUCTION

A number of therapeutic approaches have been performed for primary varicose veins of the lower extremities. Endovenous laser treatment (EVLT) is a new, minimally invasive technique for varicose veins in recent years.¹⁾ The good short-term efficacy of EVLT has been reported.²⁾ Complications after EVLT include ecchymosis, paresthesias, superficial thrombophlebitis, skin burns, pigmentation, pain, deep vein thrombosis and pulmonary embolism.^{3,4)}

A transient thrombocytosis has been found following EVLT of the great saphenous vein (GSV). This is a case report of a rare complication with a review of the literature.

CASE REPORT

A 54-year-old man with edema and pain of the left lower extremity was referred to our department. He had

not presented with any remarkable medical history or family history. His physical examination showed a body height of 174 cm, with a body weight of 62 kg; palpebral conjunctivae were neither anemic nor icteric. Left great saphenous varicose veins (clinical, etiologic, anatomic, and pathophysiologic [CEAP] classification: C3) were found. Blood test findings showed no remarkable abnormalities. The white blood cell count (WBC) and C-reactive protein (CRP) were normal at $5800/\text{mm}^3$ and 0.07 mg/dL, respectively, prior to the EVLT procedure (Fig. 1). Thrombin-antithrombin III complex (TAT) and D-dimer were within normal limits.

Ultrasonography on his lower extremity revealed the diameter of the left GSV was 14 mm, and reflux was observed in the left saphenofemoral junction (SFJ). Air plethysmography showed a pretreatment venous filling index (VFI) of 6.3 mL/sec.

Endovenous laser treatment was conducted using a 980-nm semiconductor laser ELVeS® (biolitec AG, Germany) under local anesthesia (tumescence local anesthesia [TLA] with 0.2% lidocaine). The knee was punctured with an indwelling needle. A 5 French long sheath was inserted into the GSV over a guidewire, and the tip was advanced near the SFJ. After insertion of a laser probe into the sheath, a 12-Watt (W) laser beam was continuously delivered over the length of 33 cm of the saphenous vein for 82.5 seconds from 19 mm distal to the SFJ. Cumulative exposure was 1042 Joule (J), and total time

Department of Vascular Surgery, Sendai Hospital of East Japan Railway Company, Sendai, Miyagi, Japan

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Corresponding author: Hiromitsu Sugawara, MD. Department of Vascular Surgery, Sendai Hospital of East Japan Railway Company, 1-1-5 Itsutsubashi, Aoba-ku, Sendai, Miyagi 980-8508, Japan

Tel: +83-22-266-9671, Fax: +83-22-380-2355

E-mail: hiromitsu-sugawara@jreast.co.jp

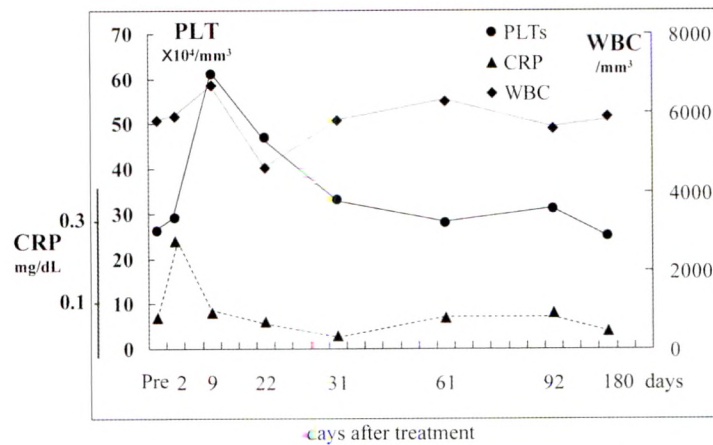


Fig. 1 Changes in platelet counts, white blood cell counts, and C-reactive protein levels after treatment. WBC, white blood cell count; PLT, platelet count; CRP, C-reactive protein; Pre, preoperative

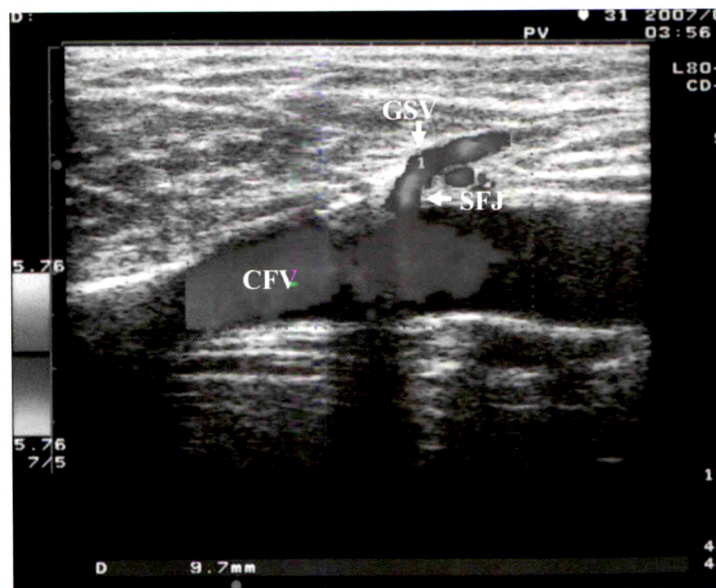


Fig. 2 Ultrasonographic image immediately after endovenous laser treatment, showing incomplete occlusion of the great saphenous vein up to the level of the SFJ. SFJ, sapheno-femoral junction; CFV, common femoral vein; GSV, great saphenous vein

of operation was 32 minutes. Color Doppler ultrasonography immediately after the irradiation revealed a patent superficial epigastric vein with blood flow blocked at a site 9.7 mm distal to the SFJ (**Fig. 2**). These procedures were conducted in a 1-day surgical setting.

during his visit on the second postoperative day, he presented with ecchymosis of the left femoral region without inflammatory findings, such as superficial

thrombophlebitis.

Color Doppler ultrasonography revealed occlusion of the superficial epigastric vein and complete thrombotic occlusion of the great saphenous vein beginning at the SFJ. There was no protrusion of thrombus inside the femoral vein. The platelet count was 292000 /mm³.

The WBC was almost unchanged at 5900 /mm³, while the CRP slightly increased to 0.24 mg/dL, albeit

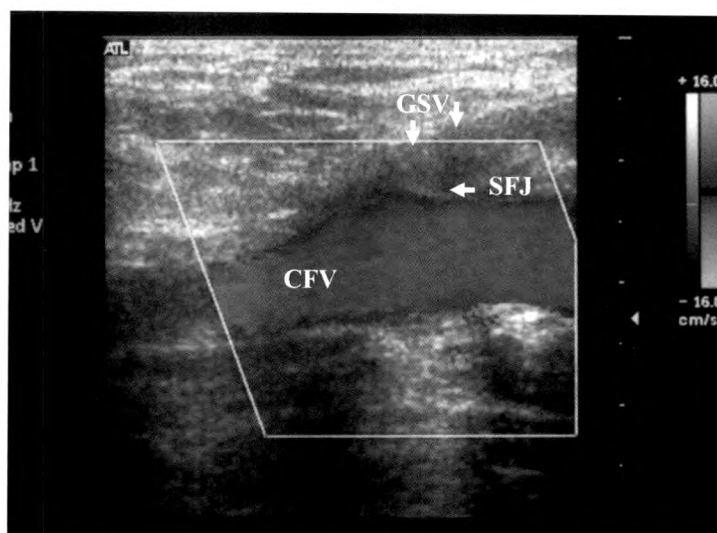


Fig. 3 Ultrasonographic image 9 days after endovenous laser treatment, showing complete occlusion of the great saphenous vein up to the level of the SFJ. The thrombus did not extend to the femoral vein. SFJ, sapheno-femoral junction; CFV, common femoral vein; GSV, great saphenous vein

within the normal range, as compared with baseline values (**Fig. 1**).

On the 9th postoperative day, marked thrombocytosis was observed with a platelet count of $610000/\text{mm}^3$. The WBC was $6700/\text{mm}^3$, and CRP was 0.08 mg/dL , both of which were within the normal ranges (**Fig. 1**). No remarkable inflammatory findings, such as superficial thrombophlebitis were observed.

Ultrasonography revealed the same findings as those observed previously: occlusion of the superficial epigastric vein, complete thrombotic occlusion of the great saphenous vein beginning at the SFJ, and no protrusion of thrombus inside the femoral vein (**Fig. 3**).

Test results for TAT and D-dimer were normal, and no respiratory symptoms were observed. By 2 months, the platelet count had returned to normal (**Fig. 1**).

Three months after surgery, air plethysmography revealed a normal VFI. No recurrence has been noted for 1 year after surgery.

DISCUSSION

Thrombocytosis is a physiological or pathological increase in the platelet count from $400000/\text{mm}^3$ or higher.⁵⁾ Thrombocytosis is classified into 3 types: myeloproliferative disorder, reactive thrombocytosis, and familial thrombocytosis. A search for causes revealed that reactive thrombocytosis constituted the largest pro-

portion of cases at 82%, whereas myeloproliferative disorder accounted for only 14% of the cases.⁶⁾ In our patient, myeloproliferative disorder and familial thrombocytosis were ruled out by family history and clinical course. Reactive thrombocytosis was considered most likely. Since platelet recovery required approximately 2 months, this reactive thrombocytosis did not appear to have been a result of outflow from the platelet storage pool after exercise or administration of epinephrine. It was probably caused by increased platelet production.

Reactive thrombocytosis can be associated with a wide variety of underlying diseases, and there have been reports of local interleukin (IL)-6 production due to photocoagulation for retinopathy⁷⁾ and increased serum IL-6 in approximately 80% of the patients with reactive thrombocytosis.⁸⁾ Serum IL-6 was not measured in our patient, though it appeared that the thrombocytosis had been triggered by increased inflammatory cytokine IL-6, which is secreted in response to tissue disorder caused by heat injury from laser irradiation.

A CRP elevation, albeit slight in degree, was observed on the second postoperative day (**Fig. 1**). CRP is a protein induced by IL-6 in the liver. IL-6 might have been produced as inflammatory reactions to laser irradiation, resulting in thrombocytosis. However, since the increased CRP value was within the normal range, other reasons cannot be entirely ruled out.

There was only 1 report⁹⁾ on thrombocytosis associated

with leukocytosis and hyperkalemia after intralesional laser photocoagulation (ILP) for vascular malformation, but no reports on thrombocytosis after EVLT for primary lower-extremity varicose vein. In the reported case of post-ILP thrombocytosis, a 1064-nm Nd:YAG laser was used with a laser power of 15 W and radiation energy of 51150 J. This treatment was presumed to have caused much more severe tissue disorder from heat injury than that in our patient, and release of potassium, an intracellular electrolyte, due to the extensive tissue destruction probably resulted in concomitant hyperkalemia and leukocytosis. In this case, the platelet count became normalized 6 days after surgery, whereas the thrombocytosis in our patient persisted for 2 months after surgery. The prolongation of thrombocytosis for as long as 2 months after the procedure might be due to distribution of the products of tissue damage over the entire body through the general circulation, which were produced by laser irradiation in the vein close to the general circulation.

Generally, in patients with reactive thrombocytosis, the platelet count does not exceed $1000000/\text{mm}^3$, and secondary thrombosis is unlikely to occur.¹⁰⁾ In our patient as well, the maximum count was $610000/\text{mm}^3$, and no other thrombosis was observed. He recovered during follow-up without use of drugs such as Bayaspirin (aspirin) with a good prognosis.

CONCLUSION

We experienced a case of transient thrombocytosis after endovenous laser treatment for primary varicose veins of the lower extremity. This is the first case report of such an event in the literature. The patient recovered after the follow-up period of 2 months with a favorable prognosis.

REFERENCES

- 1) Navarro L, Min RJ, Bone C. Endovenous laser: a new minimally invasive method of treatment for varicose veins-preliminary observations using an 810nm diode laser. *Dermatol Surg* 2001; **27**: 117-22.
- 2) Perkowski P, Ravi R, Gowda RC, Olsen D, Ramaiah V, Rodriguez-Lopez JA, et al. Endovenous laser ablation of the saphenous vein for treatment of venous insufficiency and varicose veins: early results from a large single-center experience. *J Endovasc Ther* 2004; **11**: 132-8.
- 3) Puggioni A, Kalra M, Carmo M, Mozes G, Gloviczki P. Endovenous laser therapy and radiofrequency ablation of the great saphenous vein: analysis of early efficacy and complications. *J Vasc Surg* 2005; **42**: 488-93.
- 4) Mozes G, Kalra M, Carmo M, Swenson L, Gloviczki P. Extension of saphenous thrombus into the femoral vein: a potential complication of new endovenous ablation techniques. *J Vasc Surg* 2005; **41**: 130-5.
- 5) Kuwana M. Quantitative platelet abnormality. In: Asano S, Ikeda Y, Uchiyama T, ed. *Miwa's hematology*. 3rd ed. Tokyo: Bunkodo; 2006: 1648-9. (in Japanese)
- 6) Buss DH, Cashell AW, O'Connor ML, Richards F 2nd, Case LD. Occurrence, etiology, and clinical significance of extreme thrombocytosis: a study of 280 cases. *Am J Med* 1994; **96**: 247-53.
- 7) Shimura M. Forefront of retinopathy therapy: looking at photocoagulation for diabetic retinopathy. *Folia Ophthalmol Jpn* 2007; **58**: 525-31. (in Japanese)
- 8) Tefferi A, Hoagland HC. Issue in the diagnosis and management of essential thrombocythemia. *Mayo Clin Proc* 1994; **69**: 651-5.
- 9) Fisher DM, Chang CJ, Chua JJ, Chen YR, Achauer BM. Potential complications of intralesional laser photocoagulation for extensive vascular malformations. *Ann Plast Surg* 2001; **47**: 252-6.
- 10) Schafer AI. Thrombocytosis and thrombocythemia. *Blood Rev* 2001; **15**: 159-66.

► Case Report ◀

A Combined Open and Endovascular Approach to Treat a Persistent Sciatic Artery Aneurysm in an Obese Patient

Mahim Malik, MD, Peter Fischer, MD, and Alim Khandekar, MD

Persistent sciatic artery is a relatively uncommon peripheral vascular malformation of the lower extremity arterial blood supply that is often misdiagnosed. We present a case report of a 52-year-old, obese female who presented to our center with symptoms of lower extremity ischemia. We describe a novel approach combining open and endovascular techniques for the treatment of a persistent sciatic artery aneurysm, providing maximal benefit, while minimizing potential complications due to her co-morbidities.

Key words: persistent sciatic artery, endovascular intervention

INTRODUCTION

The sciatic artery is a remnant of the lower limb circulation in the early embryonic period and is a direct branch of the umbilical artery.¹⁾ Generally, this artery involutes as the femoral circulation from the internal iliac artery develops. However, rarely this sciatic artery persists and is the main supply of blood to the lower leg. This persistent sciatic artery (PSA) has an overall incidence of 0.025%–0.04%.^{2, 3)} Complications arising from this aberrant circulation include aneurysm formation, thrombosis, as well as Rupture.⁴⁾ Multiple treatment modalities have been utilized for management of these complications, ranging from ligation to endovascular interventions. We report a case of a 52 year-old lady who presented with a pulsatile buttock mass and lower limb ischemia who was found to have a PSA. We utilized a combined open and endovascular approach secondary to her obesity to offer her the best treatment with lowest morbidity.

Health Science Center, Univeristy of Tennessee, Memphis, Tennessee, USA

Received: November 7, 2010; Accepted: March 17, 2011
Corresponding author: Mahim Malik, MD. Department of Surgery, Heath Science Center, Univeristy of Tennessee, Memphis, Tennessee, USA
Tel: +1-901-448-7635, Fax: +1-901-448-7036
E-mail: mmalik4@uthsc.edu

CASE

A 52-year-old female presented to the hospital complaining of a two-day history of left foot pain. The patient stated the pain was primarily localized to her toes. Her foot was warm; however, she did not have palpable DP or PT pulses. She was admitted, placed on a heparin drip, and a computed tomogram was obtained (Fig. 1). The imaging revealed a PSA aneurysm providing the only inflow to the above- knee popliteal artery. The common femoral artery was patent below the inguinal ligament and fairly large.

After review of the patient's films and exam, a bypass procedure was chosen to treat the PSA aneurysm. However, the more common approach to bypass from the iliac to the above-knee popliteal with proximal and distal ligation of the PSA was not selected. To perform this procedure would have required an abdominal incision underneath the patient's large pannus which almost ensured a wound infection and possible subsequent graft infection. Therefore, the patient was taken to the operating room where a femoral to above-knee popliteal bypass was performed using reverse saphenous vein graft. The distal end of the PSA was also ligated after the completion of the distal anastomosis, and the arteriogram showed good inflow to the lower leg (Fig. 2). On the first post-operative day, the patient was taken to the endovascular suite where arterial occlusive devices were placed to exclude the aneurysm proximally (Fig. 3). The patient recovered well and was discharged home after four days.



Fig. 1 Computed tomography of the left leg showing the persistent sciatic artery aneurysm and the femoral arteries.

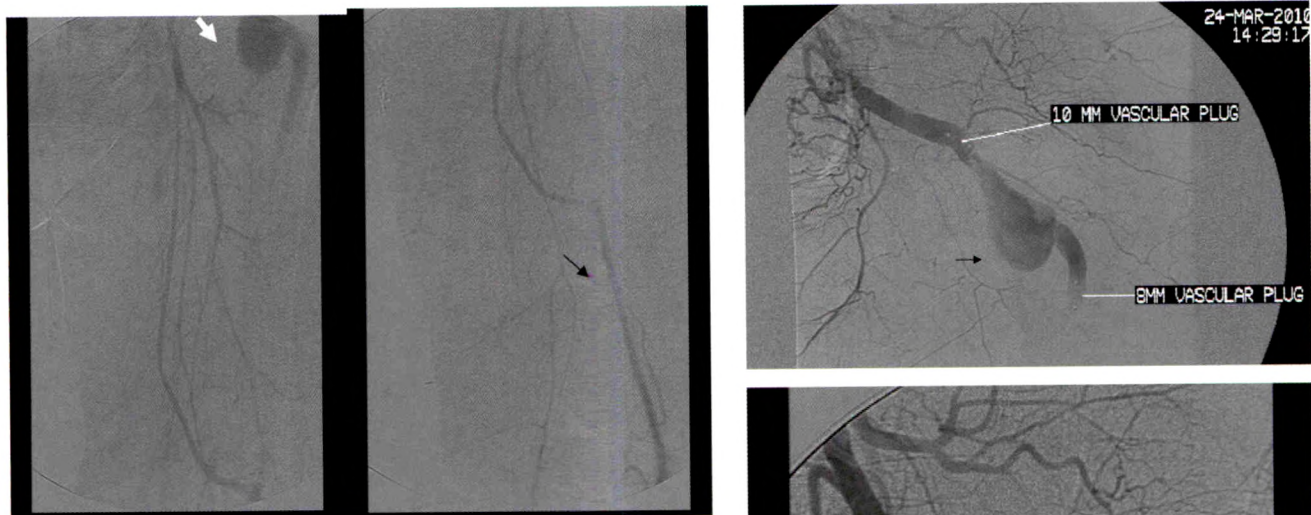


Fig. 2 Completion arteriogram of femoral to above-knee popliteal bypass.

DISCUSSION

Persistent sciatic arteries most commonly present with aneurysmal formation, reported in up to 42% of Patients.^{1, 5)} This may be complicated by thrombosis or rupture, which is contributed to congenital hypoplasia of the artery. Anatomically, the artery arises from the umbilical artery and runs along the dorsal aspect of the lower limb, giving rise to the popliteal, peroneal and tibial arterial systems. The femoral system arises from the external iliac artery, and by the third month of gestation, it coalesces with the sciatic artery, to become the dominant arterial supply of the lower extremity. At this time, the sciatic artery regresses, leaving behind only the external gluteal artery and the artery of the of the sciatic



Fig. 3 Pre and post endovascular exclusion of PSA aneurysm. (black arrow pointing at aneurysm)
PSA, persistent sciatic artery

nerve.⁶⁾ Anatomic variations in the persistent sciatic artery depend on this process of involution.

Clinically, the patient usually presents with a pulsatile buttock mass, with or without acute ischemic pain. This may result in a misdiagnosis of atherosclerotic occlusive

disease of the lower limb, leading to unnecessary procedures that do not resolve the patient's symptoms. Digital subtraction arteriography (DSA) continues to be the gold standard for imaging, but CTA and MRA have also been used for this Purpose.⁶⁾ DSA often fails to show the relation of the anomaly with the surrounding structures, leading to a misdiagnosis.⁷⁾ Promising results were shown in 2005, when Jung et al. proposed using a multidetector row spiral computed tomography (CT) scanner, scanning from the iliac bifurcation to the feet.⁷⁾ This can be used as a single modality, since with 3D reconstruction, it is possible to define the anatomic relations as well distal out-flow vessels.

Definite management of a persistent sciatic artery is warranted in symptomatic patients. Due to the multiple anatomic variations, treatment options need to be tailored according to the type of PSA, the femoral circulation, presence or absence of aneurysmal disease and/or concomitant vascular occlusive disease. PSA aneurysms have been managed by both open and endovascular techniques.⁸⁻¹⁰⁾ Ligation of aneurysm via transgluteal approach has been described; however, this may lead to critical lower limb ischemia in the case where the PSA is the sole blood supply.⁴⁾ Therefore, some sort of a revascularization procedure must be employed, as well. This may be difficult if the femoral vessels are hypoplastic. The obturator bypass approach employed by Urayama et al. is a viable option but presents technical difficulties especially in an obese patient.¹¹⁾ Endovascular approaches have been used, including deployment of stents and coil embolizations.¹²⁾ However, the long-term results of these are largely unknown, and the anatomic position of the aneurysm exposes the risk of trauma, fracture and embolization of the devices when the patient sits. Persistent sciatic arteries present a risk of recurrence due to the presence of feeder vessels inside, thereby making simple exclusion more likely to result in failure.^{12, 13)}

CONCLUSION

We described a combined open and endovascular approach to treat a PSA aneurysm. The open femoral to popliteal bypass provides the best revascularization to the leg with the opportunity to distally ligate the PSA. The success of this procedure depends on the size of the femoral arteries and might not be possible if they are

severely hypoplastic. The endovascular approach to proximally ligate the PSA avoids the abdominal incision that in this patient would be placed underneath her large pannus. This combination procedure should provide similar results as an iliac bypass without wound morbidity in this obese patient.

REFERENCES

- 1) Brantley SK, Rigdon EE, Raju S. Persistent sciatic artery: embryology, pathology, and treatment. *J Vasc Surg* 1993; **18**: 242-8.
- 2) Mousa A, Rapp Parker A, Emmett MK, AbuRahma A. Endovascular treatment of symptomatic persistent sciatic artery aneurysm: a case report and review of literature. *Vasc Endovascular Surg* 2010; **44**: 312-4.
- 3) Mandell VS, Jaques PF, Delany DJ, Oberheu V. Persistent sciatic artery: clinical, embryologic, and angiographic features. *AJR Am J Roentgenol* 1985; **144**: 245-9.
- 4) Bower EB, Smullens SN, Parke WW. Clinical aspects of persistent sciatic artery: report of two cases and review of the literature. *Surgery* 1977; **81**: 588-95.
- 5) Williams LR, Flanigan DP, O'Connor RJ, Schuler JJ. Persistent sciatic artery. Clinical aspects and operative management. *Am J Surg* 1983; **145**: 687-93.
- 6) Abularrage CJ, Crawford RS, Patel VI, Conrad MF. Diagnostic strategies for the persistent sciatic artery. *Vasc Endovascular Surg* 2009; **43**: 485-9.
- 7) Jung AY, Lee W, Chung JW, Song SY, Kim SJ, Ha J, et al. Role of computed tomographic angiography in the detection and comprehensive evaluation of persistent sciatic artery. *J Vasc Surg* 2005; **42**: 678-83.
- 8) Hutchinson JE 3rd, Cordice JW Jr, McAllister FF. The surgical management of an aneurysm of a primitive persistent sciatic artery. *Ann Surg* 1968; **167**: 277-81.
- 9) Becquemin JP, Gaston A, Coubret P, Uzzan C, Melliere D. Aneurysm of persistent sciatic artery: report of a case treated by endovascular occlusion and femoropopliteal bypass. *Surgery* 1985; **98**: 605-11.
- 10) Wijeyaratne SM, Wijewardene N. Endovascular stenting of a persistent sciatic artery aneurysm via retrograde popliteal approach: a durable option. *Eur J Vasc Endovasc Surg* 2009; **38**: 91-2.
- 11) Urayama H, Tamura M, Ohtake H, Watanabe Y. Exclusion of a sciatic artery aneurysm and an obturator bypass. *J Vasc Surg* 1997; **26**: 697-9.
- 12) Steele G Jr, Sanders RJ, Riley J, Lindenbaum B. Pulsatile buttock masses: gluteal and persistent sciatic artery aneurysms. *Surgery* 1971; **82**: 201-4.
- 13) Batchelor TJ, Vowden P. A persistent sciatic artery aneurysm with an associated internal iliac artery aneurysm. *Eur J Vasc Endovasc Surg* 2000; **20**: 400-2.

The 4th Annual Meeting of World Federation of Vascular Societies

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Symposium

CAN WE WORK TOGETHER TO DEVELOP RESOURCES TO SUPPORT OUR VASCULAR TRAINING PROGRAMS?

Robert A Fitridge

Australian & New Zealand Society for Vascular Surgery
The University Of Adelaide, Discipline of Surgery and Vascular Surgery Unit, The Queen Elizabeth Hospital, Woodville SA, Australia

As vascular surgery has become an independent specialty, formal curriculum development has become mandatory. This has also required definition of competencies expected of vascular spe-

cialists.

Appropriate resource material is required to support the curricula. The sharing of appropriate resource material should be advantageous to each country's training program.

This presentation will give an overview of current vascular curriculum resources and possible options for further collaboration.

Balancing Training between Open and Endovascular Approaches

John Wolfe

St Mary's Hospital, United Kingdom

Current problems for vascular surgery training in Japan

Tadahiro Sasajima

Department of Surgery, Asahikawa Medical University, Asahikawa, Japan

Abstract

After graduation of 6 year medical school, and the national board exam every doctor must receive 2 year-general practice training in duty. After the 2 years, they are majoring vascular surgery. The Japanese Board of Cardiovascular Surgery was developed in cooperation with the Japanese Association of Thoracic Surgery, Japanese Society for Cardiovascular Surgery, and Society for Vascular Surgery on March, 2004, and the board certified subspecialty system for cardiovascular surgery has started from April, 2004. In the system, vascular surgery specialists are officially not separated from cardiac surgery specialists, and fellows require cardiovascular surgery training for the subspecialty board exam including cardiac surgery. In qualification for the Board Exam, vascular surgery fellows must experience different types of operations in the following Board designated cardiovascular operations: operations are scored by the difficulty levels; category A, 3 points; B, 4 points, and C, 5 points, and the minimum requirement of total points are 500, which must include points of 50 cases as an operator and 50 cases as a first assistant. In 2009, 100 of 139 qualified surgeons passed the exam, and there are 1667 Board Certified Cardiovascular Surgeons at the present time. Meanwhile, numbers of patients underwent vascular surgery (except venous surgery) in 360 certified hospitals were 31,890 in 2008 in Japan, and annual numbers of arterial operations were only 30 cases in 33% of 360 hospitals.

In conclusion, problems should be solved in vascular surgery

training in Japan

1. Separation of vascular surgery specialist from the Board Certified Cardiovascular Surgeon is necessary for improving the quality of vascular surgery training.

2. There is obvious mismatch of patient volume and vascular surgery specialists for effective training, and so it will be necessary to reduce numbers of cardiovascular surgeons as well as certified institutes.

Vascular Surgery in the United States: Development of New Training Paradigms and Curricula

Joseph L. Mills, Sr., M.D.

Vascular and Endovascular Surgery, University of Arizona Health Sciences Center, United States of America

Training curriculum to be vascular surgeon including endovascular procedure

Shoei-Shen Wang

Department of Cardiovascular Surgery, National Taiwan University, Taipei, Taiwan.

In Taiwan, vascular surgery is traditionally a component of cardiovascular surgery, not general surgery. The objective of training is that every vascular surgeon has sufficient knowledge and skill to manage vascular lesions. There are four major components in vascular training: 1. Diagnostic vascular lab: ultrasound imaging, non-invasive vascular examination (ABI, PVR, MVO etc) and angiographic examination in hybrid operation room. 2. Vascular clinic: pharmacologic therapy, risk factors modification (DM, hypertension, hyperlipemia, arrhythmia such as atrial fibrillation). 3. Vascular surgery: bypass grafting, creation of arterio-venous fistula, phlebectomy for varicose vein. 4. Endovascular therapy: aortic stent grafting (EVAR, TEVAR), transluminal angioplasty for PAD or AVF, IVC filter placement, endovascular venous therapy.

To finish the endovascular training, we must perform more than 150 cases in peripheral vascular surgery, 10 cases in aortic or vena caval surgery, 5 cases in endovascular aneurysm repair, 200 cases in vascular lab and duplex studies, 100 cases in catheterization laboratory, and we must finish the training course in aortic stenting. It is essential to publish more than one articles in SCI journals. We have published several textbooks including "Vascular Surgery", "Cardiovascular Surgery", "Vascular Operations", and "Vascular Guidelines".

In Taiwan, we performed the first clinical trial on endovascular stent for abdominal aortic aneurysm repair (EVAR) at the National Taiwan University Hospital (NTUH) in 2002. Because of our good clinical result, the Department of Health (DOH) of Taiwan released the clinical trial of EVAR in 2005, and it is allowed to perform endovascular stent-grafting for thoracic aortic repair with no necessity to perform clinical trial on Oct. 25, 2006. In Taiwan we did the first endovascular stent-grafting for thoracic aortic repair at NTUH on Nov. 13, 2006.

On September 11, 2005, we founded Taiwan Society for Vascular Surgery (TSVS) to promote the knowledge of vascular surgery and the wisdom to manage and prevent the vascular diseases. In September 2007, we held the Asian chapter of International Union of Angiology (IUA) to provide the chance for the outstanding vascular surgeons and allied specialists to meet together to exchange their knowledge and wisdom. We are going to hold the 12th Asian Society for Vascular Surgery (ASVS) in Taipei, Taiwan in September, 2011.

PELVIC CONGESTION SYNDROME MANAGEMENT IN ORIENT

Al Tarazi^{L1+2}, Kabani I², Hassan AM²

¹Damascus University Hospital, Syria. ²Arabe Endovascular Group

Aim. Pelvic Congestion Syndrome (PCS) is an overlooked and under diagnosed common gynecologic and vascular pathology and a major cause of women's invalidism and both sex postsurgical varices recurrence. Few epidemiological studies have been carried out due to false perception that it is not really a major problem. Some studies in USA & Europe showed that one-third of all women will experience some chronic pelvic pain during their lifetimes; PCS presents 25.0% of all consultation in gynecology. Pathologies, anatomy, clinical aspects, imagery (echo Doppler, MRI, contrast CT and Laparoscopy), our treatment methods (medical, surgical and endovascular including our own sclerotherapy method) are summarized. The aim of this cross sectional and multicentric study was to evaluate the prevalence of PCS in genital activity aged Syrian women; how to approach this problem considering the oriental mentality and the sensibility to inquire about such somehow sex related subject.

Methods. The study was carried out through 22 Primary Health Care

(PHC) centers, in three main Syrian departments: Damascus, Latakia (the coast), Dair el Zor (eastern desert). Every other Syrian woman visiting the selected PHC centers during one month, for any reason, aged 18-48 years was eligible for the study. All doctors (mostly females) participated in the study in the 3 departments were trained by the same trainer; filling the questionnaire, performing full clinical examination.

Results. Only 2023 (out of 3544 recruited) participants were included.

(The others excluded for inadequate cooperation or missing data). Global Results; 47% of participants complain of some clinical aspects of PCS; only 22% of suffering women have ever consulted; very rarely PCS diagnosis was established.

Conclusion. Higher prevalence of PCS in Syrian female population than in Western countries maybe due to High number of pregnancies in Syria and to the style of life. Difficulties to approach PVC with young Syrian women due to traditional taboos. Gynecologists often wrongly attribute PVC symptoms to some psychological or local neural ambiguous reasons.

Vascular Surgery Training Curriculum and Proposals from India

Prof Kumud Rai

Max Heart & Vascular Institute, India

There is a strong felt need amongst vascular surgical societies of the world to have a unified training curriculum for surgeons training to be vascular surgeons. In the rapidly shrinking world people relocate from one continent to another and is obviously important to have some sort of uniformity of training standards across the world.

Vascular surgery training in India is for three years (after basic surgical training). At present 8 universities / hospitals conduct the training for the degree of either MCh (Master of Chirurgie), or DNB (Diplomate of National Board). There is a prescribed syllabus/curriculum covering all aspects of vascular disease. Most of the training is hands-on, and the student is expected to submit a short thesis on a vascular topic before he can take the exit exam. Students are rotated through departments of Radiology (for training in Ultrasound), and either interventional cardiology or interventional radiology for training in endovascular procedures (in those training institutions where they are not being performed by vascular surgeons). The formal exit exam consists of a written test as well as a practical examination. Operative skills are not assessed.

There is a need to revamp this curriculum and align it in line with the proposed uniform international curriculum (IC). Fitridge et al have worked on the IC and published their ideas in a recent issue of the Eur J Vasc Endovasc Surg. Concrete proposals regarding the curriculum and its duration, number and nature of open & endovascular procedures, resource materials, use of simulators for learning endovascular skills, nature and conduct of the exit examination etc., should be discussed at the WFVS meeting 2020 at Kyoto so that the participating societies can agree on this important matter, and implement it in their countries / regions in a phased manner.

Endovascular training in a resource constrained health care system

Martin Veller on behalf of the Vascular Society of Southern Africa University of the Witwatersrand, Johannesburg, South Africa

All health care training in South Africa occurs in the public health care sector which is funded exclusively from government coffers and equates to less than 400 US\$ spent on health care per person. On the other hand, the other 15 million inhabitants of South Africa are treated in a fee for service private sector, mostly funded by mutual insurance schemes, where the amount spent is substantially greater (2.5 times more).

As a consequence, the focus in the public health care sector is largely to address basic health care needs and although limited access to specialist and sub-specialist medical services is available these are usually severely under funded. The well funded private health care sector however demands, and can generally afford high of level specialist and subspecialist services.

Training in most aspects of endovascular treatment is therefore required to ensure that the wide variety of service demands of the countries population is met. Since the high costs of many of the endovascular technologies are not affordable in the public sector, innovative solutions to this dilemma have to be found.

Currently, South African trainee vascular surgeons are receiving inadequate exposure to endovascular therapies. To address this deficiency in vascular surgical training, the Vascular Society of Southern Africa is:

- Defining the exposure needed by trainees to acquire appropriate endovascular skills by evaluating the experience in other countries and modifying this to the South African disease profile. A curriculum will be developed based on these findings.

- Cost saving endovascular technologies will be used whenever possible in the current training programmes. For example, balloon angioplasty of iliac arteries with selective use of stents and subintimal approaches can be used without limitation. As a consequence all vascular surgical trainees are competent in this aspect of therapy at the completion of their training.

- Accrediting endovascular units in the private sector in which the full spectrum of endovascular procedures are performed for training purposes.

In conclusion, despite significant resource limitations, it is possible to train vascular surgeons to acquire appropriate endovascular skill ensuring that they are able to meet the health care demands of the society in which they work.

Free Paper Session

Relationship of serum ferritin, cholesterol, and intimal hyperplasia after mechanical injury to carotid artery in a rat model

SD KIM, SC PARK, JI KIM, SS YUN, IS MOON

Division of Vascular & Endovascular Surgery, Department of Surgery, College of Medicine, The Catholic University of Korea, Seoul, Korea

Purpose: Iron has an important role in the process of oxidizing the Low Density Lipoprotein in the arterial wall during the development of atherosclerosis, but the role of iron during the development of intimal hyperplasia has been not confirmed. Therefore, we evaluated the relationship of serum ferritin, serum cholesterol and intimal hyperplasia.

Methods: Forty rats were divided in four groups according to diets. At the sixth week, we induced clamping injury at the left common carotid artery of each rat. At the end of the eighth week, we obtained the tissue of the left common carotid artery from each rat, and we performed staining. After that, we evaluated the differences of the thickness of the arterial walls according to the groups

Results: Arterial thickness was significantly increased from group I (normocholesterol and normoferritin group) to group IV (hypercholesterol and hyperferritin group) respectively ($P < 0.001$). For the intimal thickness, intimal thickness of group II (hypercholesterol and normoferritin group) was thicker than that of group I ($P < 0.001$), and intimal thickness of group IV was thicker than that of group II ($P < 0.001$), and there was no significant difference between group II and group III (hypercholesterol and hypoferritin group) ($P = 0.124$) for the intimal thickness.

Conclusion: We suggest the possibility that serum ferritin and hypercholesterolemia are proportionally related with intimal hyperplasia. But we think that large-volume experiments in animal models and prospective studies in human are needed to confirm and expand on our results.

Parental Occurrence of Intermittent Claudication is an Independent Risk Factor for Intermittent Claudication in Adult Offspring: The Framingham Heart Study

Alik Farber MD,

Section of Vascular and Endovascular Surgery, Boston Medical Center, Boston, Massachusetts, United States of America

Introduction: Peripheral arterial disease (PAD) affects ~8 million people in the United States. Studies suggest that there is an inherited component of PAD; however, no study has quantified the extent to which these influences are independent of risk factors. Our objective was to prospectively examine whether intermittent claudication (IC) in parents increased risk for IC in adult offspring independent of established cardiovascular risk factors.

Methods: The study sample consisted of offspring participants aged >30 years with both parents enrolled in the original cohort of the Framingham Heart Study and free of cardiovascular disease (CVD) at three baseline examinations (n= 2970 unique participants, 53% women). In both parents and offspring, IC was adjudicated by a panel of three investigators and defined as exertional cramping discomfort in the calf appearing sooner with rapid or uphill walking and relieved with rest. Data from the three exams, each with 12 years of follow-up were pooled. Cox proportional hazards regression was used to examine the 12 year risk for incident IC in offspring associated with parental IC adjusting for age, sex, diabetes, smoking, systolic blood pressure, anti-hypertensive treatment, total cholesterol, and HDL cholesterol. In secondary analysis we additionally adjusted for interim CVD.

Results: Among 909 person-exams in the parental IC history group (mean age 49.9 years) and 5397 person-exams in the no parental IC history group (mean age 47.6 years) there were 101 incident IC events during follow-up. Baseline risk factors were more prevalent in the parental IC group compared with the no parental IC group. Parental history of IC significantly increased the risk of incident IC in offspring (multivariable adjusted hazard ratio of 1.81, 95% CI 1.14, 2.88). There was no change with adjustment for interim development of CVD (multivariable adjusted hazards ratio 1.81, 95% CI 1.14, 2.86).

Conclusion: IC in parents increases risk for IC in adult offspring independent of established risk factors. These data suggest that there is a genetic component of PAD and support future research into genetic causes.

COMBINATION OF EDARAVONE AND TRANSVERTEBRAL COOLING PAD REDUCE SPINAL CORD ISCHEMIA-REPERFUSION INJURY

Bagus Herlambang, Kazumasa Orihashi,

Shinya Takahashi, Taketomo Mizukami, Taijiro Sueda

Hiroshima University, Hiroshima, Japan

Purpose: Spinal cord injury following thoracoabdominal aortic surgery remains a devastating event. Many reports show that free radicals play some role in inducing ischemia-reperfusion injury. Hypothermia has been recognized as a physical adjunctive therapy against ischemic injury. We examined combined protective effect of edaravone, a free radical scavenger, and transvertebral cooling pad against spinal cord ischemia-reperfusion injury in a rabbit model.

Methods: Spinal cord ischemia was induced by applying vascular clamp on the aorta distal to renal artery and proximal to aortic bifurcation for 30 minutes. Eighteen rabbits were divided into three groups (six in each group): Group I with edaravone (4°C, 1mg/kg) infused into the clamped segment of the aorta; Group II with cooling pads placed on the vertebra following aortic clamping in order to keep the temperature of vertebral bone within 25-30 °C; Group III with both of them. Postoperative assessments included Tarlov score at 8, 24, and 48 hours, histopathology of spinal cord, and measurement of malondialdehyde levels in the spinal cord.

Results: At 48 hours postoperatively, Tarlov score in Group I, II, and III was 1.7 ± 1.0 , 1.5 ± 1.1 , and 4.0 ± 0.0 (mean $\pm$ SD), respectively ($p < 0.01$). Total number of motor neurons in anterior horn of the spinal cord was significantly higher ($p < 0.001$) in Group III (55.6 ± 2.8) than Group I (30.8 ± 5.7) and Group II (28.8 ± 5.3). Malondialdehyde level in Group III (23.0 ± 5.9 nmol/ml) was significantly lower ($p < 0.001$) than Group I (68.0 ± 5.8 nmol/ml) and Group II (64.1 ± 8.8 nmol/ml).

Conclusions: Edaravone infused into the clamped segment of aorta combined with transvertebral cooling pad was effective in reducing ischemia-reperfusion injury of spinal cord during aortic clamping.

NEW SOMATIC MUTATIONS IN EXON 17 OF ANGIOPOIETIN RECEPTOR GENE TEK WERE IDENTIFIED IN VASCULAR ANOMALIES

Caisheng Ye, Lingxiao Pan, Runyi Ye, Xiaoxi Li, Shenming Wang

the first affiliated hospital of Sun Yat-sen University, Guangzhou, China

Purpose:

We assessed whether somatic mutations in exon 17 of the endothelial cell tyrosine kinase receptor Tie-2 (encoded by TEK) had a role in the vascular anomalies and investigated the possible biological consequence of the mutations.

Methods:

Direct sequencing of PCR-amplified DNA, extracted from 140 lesions in 129 individuals and 33 samples in control, was used for detecting the mutations in exon 17 of the TEK gene, confirmed by allele-specific PCR. The expressions of p-Akt (Thr308) were measured by immunohistochemical staining in 129 cases of vascular anomalies and 12 specimens of normal tissues. Likewise, the expressions of Tie-2 and Angiopoietin-1 (Ang1) were measured in 50 cases of vascular anomalies and 12 specimens of normal tissues.

Results:

Seven somatic TEK mutations (L914F, R915C, Y897C, Y897H, S917L, R918H, R918C), of which R918H and R918C substitutions were firstly identified, were detected in lesions from 43 (33.3%) of 129 individuals. Most of them (90.7%) were single substitution. Moreover, immunohistochemical staining showed the similar expressions of Tie-2 between the mutation group and the wild type group of vascular anomalies. Ang1 expression in vascular anomalies was significantly higher ($P=0.006$) than that in normal tissues, and it was equal between the mutation group and the wild type group of vascular anomalies. Albeit p-Akt (Thr308) expression in the mutation group or the wild type group of vascular anomalies was significantly higher ($P<0.05$) than that in normal tissues, it was significantly lower ($P=0.045$) in the mutation group than that in the wild type group.

Conclusions:

Our study reveals that vascular anomalies may have somatic changes in exon 17 of the TEK gene. The activation of Akt possibly plays an important role in vascular anomalies in vivo, but the somatic mutations in exon 17 of the TEK gene weaken this effect and it may imply some additional mechanism.

Vascular Laboratory, Essential Service for Vascular Surgeons

Trab, M

Tawam Hospital, United Arab Emirates

Hypothesis:

The Noninvasive Vascular Laboratory is a modern, uniquely designed facility to serve both inpatients and outpatients and it is conveniently located in the main Hospital. The vascular laboratory now offers a vascular screening exam for the detection of arterial and venous disease. A registered vascular technologist performs examinations in the vascular Lab. Examination findings are reviewed and interpreted by vascular surgeons. This service will help physicians to detect arterial and venous diseases earlier and treat them in a specialized center of vascular surgery.

Methods:

The service of Vascular Lab was started in April 2008, two registered vascular technicians were performing the procedures and all the results were reported manually in the file of the patient, the patient were referred from the vascular clinic and from other subspecialty in the hospital, On the 15th of September 2008 we moved to the digital reporting system PACS which is implanted in our hospital we were part of it and all the tests were reported electronically through the net and reported and signed by vascular surgeons. We started 2 screening program for peripheral arterial disease for diabetic patient and surveillance program for hemodialysis access.

Results:

Between 1st of September 2008 and 1st of September 2009 we performed 4822 vascular examinations in our Vascular Lab. 1779 cases were venous studies, 1012 cases peripheral arterial studies and 1068 were cerebral arterial studies. We performed 100 vascular screening to detect early arterial diseases and 597 cases follow up cases of vascular access for hemodialysis. We also conducted 50 studies of bypass surveillance for the cases which were done in Tawam.

Conclusions:

Initiating a vascular lab is an important element in the success of vascular surgery service in a tertiary referral hospital.

The Vascular Laboratory provides clinical diagnostic testing of vascular diseases. It has an important role in teaching, training and research. The tests which were done in the vascular lab are integral to clinical decision-making in several key areas including vascular surgery, nephrology, hematology, pediatrics and Neurology

PRE-OPERATIVE DIRECT PERCUTANEOUS EMBOLIZATION OF CAROTID BODY TUMORS SOLELY WITH GLUE

Shridhar Khajindar¹, P C Gupta²

Dept of Interventional Radiology¹ and Dept of Vascular & Endovascular Surgery², CARE Hospital, Hyderabad. INDIA

Purpose

Paragangliomas are highly vascularized usually benign neoplasms arising from nerve tissue. Endovascular preoperative embolization is used to facilitate surgery but is often not complete, due to tiny feeding arteries not feasible for selective catheterization. To overcome this limitation, we report our initial experience and the efficacy of Direct Percutaneous Glue Embolisation of Carotid Body Tumor (Paragangliomas) solely with n-butyl cyanoacrylate (NBCA) and to evaluate angiographic and clinical outcome.

Methods

All three patients presented with symptomatic painful left sided neck swelling. CT and MRI scans (plain and contrast) revealed a large well defined lobulated soft tissue lesion at the bifurcation of left CCA with uniform contrast enhancement with or without causing mass effects in the form of compression of oro and nasopharynx. MRAngio showed, classical splaying of carotid bifurcation and its branches. Also they were recently diagnosed with Hypertension and on anti HTN medication. With this diagnosis of carotid body tumor, surgical excision was planned. All three patients were referred to Interventional Radiology dept. for pre operative embolisation. Procedure was done under general anaesthesia. Embolisation was performed with Glue mixed with lipiodol in different concentrations.

Result

It was a relatively bloodless surgery in all three patients. Surgical separation of tumor and its capsule from the carotid vessels & the adjacent soft tissues and the surgical excision of tumor were relatively easy. The overall blood loss during procedure was very minimal.

Conclusion

These cases are being presented to re-emphasize the role of pre operative embolisation of Carotid Body Tumor resulting in clean bloodless surgery and better patient outcome and improve patient safety.

Can intra-operative blood flow assessment predict AV Fistula maturation?

Lt Col RPS Gambhir, Maj V Dhawan

Armed Forces Medical College, Pune.

Introduction

Arteriovenous fistula (AVF) for haemodialysis access have variable maturation rates. Primary failure to mature has varied from 25-43% in recent literature, inspite of preoperative vascular mapping to select the most appropriate vessel for AVF creation. An AVF after maturity, on cannulation needs to deliver flow rates of 350-400ml/min for dialysis. The aim of this study was to assess blood flow in the AVF immediately after creation of the access, and correlate with future patency and maturation.

Methods: 150 patients aged 10 to 84 years who underwent AVF construction over a 3 year period had their blood flows measured immediately after the creation of the AVF. The patients were followed for over 1-30 months to assess primary patency and maturation rates.

Results: Radiocephalic (RC AVF) (n = 90), Brachiocephalic (BAVF) (n = 50), and 10 transposed basilic vein AVF (TBAVF) were performed. The calculated mean flow rate was 127 1000 ml/min. 11% rate of nonmaturation of RCAVFs (n = 10) was significantly greater than the 6% rate for BCAVFs (n = 3) (P < 0.05). The mean flow across the AVF in successful RC AVF and BAVF was 591 ml/min and 1000 ml/min respectively compared to 127 ml/min and 237 ml/min in the unsuccessful group (p 0.032).

Conclusion: Doppler blood flow measurements across the AVF immediately post op is significantly different among the successful and unsuccessful group. Flow rates < 150 ml/min for RCAVF and <300 ml/min for BAVF should be an indication for immediate reassessment and maybe revision.

IMPACT OF POST-THROMBOTIC SYNDROME ON QUALITY OF LIFE

Dr Siddharth Rajput¹, Dr R. Sekhar²

¹Dr Siddharth Rajput, M.B.B.S, D.N.B (General Surgery)-Post-graduate, Department of Vascular and Endovascular services, Jagjivanram Western Railway hospital, Mumbai, India.

²Dr R. Sekhar, M.S, F.R.C.S, Department of Vascular and Endovascular services, Jagjivanram Western Railway hospital, Mumbai, India.

Purpose:

The post-thrombotic syndrome (PTS) is a chronic, poorly understood and frequent complication of deep venous thrombosis (DVT), yet its impact on health-related quality of life has not been well characterized. We compared quality of life (QOL) in patients

with and without PTS, and assessed whether QOL correlated with severity of PTS. We also studied predictors of post-thrombotic syndrome.

Methods:

Study population comprised of 54 patients with documented index episode of DVT. PTS and its severity were diagnosed using a validated clinical scale. Subjects completed the quality of life questionnaire. Quality-of-life scores were compared in patients with and without PTS, and by severity of PTS. Logistic regression was used to identify predictors of post-thrombotic syndrome.

Results:

In the 54 patients (mean age, 53.18 years), the prevalence of post-thrombotic syndrome was 46.30% and that of severe PTS was 12.96%. Subjects with PTS had significantly worse quality-of-life scores than those without PTS (mean $\pm$ SD QOL score, 56.16 $\pm$ 6.20 vs 68.27 $\pm$ 4.27, respectively, $P < 0.001$), which worsened significantly with increasing severity of PTS. Homocysteinemia and reflux in deep veins were independent predictors of PTS (OR = 5.04, $P = 0.0269$ & OR = 0.10, $P = 0.0006$).

Conclusion:

Post-thrombotic syndrome has a significant impact on quality of life and our study emphasizes the need for effective prevention and treatment of the PTS. While the presence of reflux in deep veins and homocysteinemia appear to be associated with an increased risk of post-thrombotic syndrome, these findings require further evaluation in prospective studies.

Operating on patients on warfarin – a simpler alternative approach

Danny Chiu

Monash University, Easternhealth, Australia

The increasing number of patients prescribed long term warfarin creates problems for surgeons and interventionalists. The "traditional" management involving conversion to heparin for elective procedures or the use of fresh frozen plasma (FFP) and Vitamin K in emergency situations is cumbersome and problematic with issues of safety, cost, organisation and inconvenience for both patients and medical staff. We have been using an alternative method that is applicable in both elective and emergency settings, rapidly creates a "safe" operative environment yet minimises the risk of thrombotic complications. It is cost competitive to existing strategies.

We have reviewed our experience of the first 50 on Warfarin (INR 2.0 – 3.9) patients who received Prothrombinex-HT intravenously sixty minutes prior to intervention. These were patients undergoing vascular surgery or angiography and all were anti-coagulated with warfarin (INR2.0-3.9).

After receiving the Prothrombinex-HT infusion, all were fully reversed (INR1-1.3). The patient's normal dose of Warfarin was

recommenced on the night of surgery (excluding 4 patients who were nil by mouth) and these patients all returned to a stable anti-coagulated state (INR>2.0) by day 2. No complications, either bleeding or thrombotic were noted.

Our current management of anti-coagulated patients is to continue warfarin up to the time of admission, reverse immediately pre-op with Prothrombinex-HT and restart warfarin on the night of surgery. Additional heparin may be required for 24-48 hours in patients with prosthetic heart valves depending on INR levels.

Prevalence of asymptomatic atherosclerosis In high risk Arab patients with diabetes: A prospective Study.

Mohamed Amin Elsharawi

University of Dammam, University of Dammam, Saudi Arabia

Diabetes mellitus is a major risk factor for atherosclerosis and accordingly increase morbidity and mortality. This study aimed at screening of high risk diabetic patients for atherosclerosis at different territories.

Patients and methods: All high risk asymptomatic patients attended the diabetic clinic, King Fahd Hospital of the University, Saudi Arabia were invited to be screened for peripheral arterial disease (PAD), extra-cranial cerebrovascular disease (CVD) and coronary artery disease (CAD) over one year. All participants underwent measurement of ankle brachial pressure index, carotid duplex scan and exercise electrocardiography. All patients underwent evaluation of other risk factors for atherosclerosis

Results: One hundred and sixty nine patients were invited to be screened. Of these 138 (82%) completed all the screening tests. The mean age was 53.5 $\pm$ 7.18years. Seventy-five (55%) had evidence of atherosclerosis. In the atherosclerotic group, 24 patients had PAD, 47 had CVD and 30 had CAD. There were significant differences between the atherosclerotic and non-atherosclerotic groups as regard most of risk factors. In age, sex adjusted, the risk of developing atherosclerosis was significantly increased with all risk factors. Dyslipidemia had the highest association (OR 9.7, 95% CI 8.1-10.2)

Conclusion: Participation and diagnostic yield of screening for atherosclerosis had satisfactory validity and reliability. Routine screening in high-risk diabetic patients can serve as an effective tool for diagnosis of sub-clinical cardiovascular disease and provide strategies to optimize risk reduction.

Cytoreductive therapy using HSV-1 for the treatment of Intimal Hyperplasia

Christopher L. Skelly MD, Qi He MD, Lisa Spiguel MD, Bernard Roizman Sc.D, Ralph Weichselbaum MD. (No competing interests)
University of Chicago, United States of America

INTRODUCTION: Intimal hyperplasia (IH) is a leading cause of vein graft or endovascular failure when treating peripheral or coronary arterial disease. To date, genomic and proteomic strategies to reduce IH have failed to be realized clinically. The strategy of viral cytoreductive therapy is a mainstay of cancer therapies, but overlooked as a therapeutic strategy in the cardiovascular field. It has been shown in the oncology field that cells with constitutively active MEK pathway are susceptible to mutant HSV-1 resulting in cytolysis. Therefore, it was hypothesized that MEK activity in smooth muscle cells (SMC) confers susceptibility to mutant HSV-1 with a dual deletion of the γ 34.5 gene resulting in cyto-reduction in vitro and a decrease in IH in vivo.

METHODS: Two HSV-1 mutant viruses (γ 34.5 deletion) were used for all experiments: R3616 (dual deletion) and R7020 (single deletion). Cell cultures were performed using human aortic smooth muscle cells (SMCs). The appropriate dose of virus was identified with a dose response assay. An MTT assay using SMCs stimulated to proliferate in the presence of ascending doses of MEK inhibitors PD98059 or U0126 and IPFU/ml of each virus was performed with varying time points of cell survival evaluated out to 72 hours. Western blot analysis was performed to determine p-ERK1/2 activity at increasing concentrations of PD98059 or U0126. A balloon injury/low shear stress New Zealand White Rabbit model of IH was used to evaluate in vivo efficacy. Samples were compared using student t-test.

RESULTS: In vitro dose response revealed a dose dependent susceptibility to both viruses (data not shown). R7020 showed more cytolysis at lower concentrations. This was reflected in the in vivo experiments where a dose dependent reduction of IH for both R3616 and R7020 compared to control was realized (Fig 1). At 72 hours, PD98059 (5 μ M) significantly increased cell survival in cells infected with R3616 ($p < 0.00001$) and to a lesser extent R7020 ($p < 0.0001$) (Fig 1A). Further, at 72 hours U0126 (5 μ M) significantly increased cell survival from $62 \pm 7.4\%$ (virus alone) to $98 \pm 2.7\%$ (virus and U0126) ($p = 0.0002$) in cells treated with R3616 (fig 2B). There was no difference between the control ($100 \pm 2.9\%$) and the treated group ($98 \pm 2.7\%$) ($p = 0.8$).

CONCLUSION: Both in vitro and in vivo SMCs are susceptible to both HSV mutants in a dose dependent fashion. R7020 is more efficacious in blocking IH than R3616. MEK inhibition suppresses R3616's ability to lyse proliferating SMCs confirming the hypothesis that MEK activity confers susceptibility to mutant HSV-1 with a dual deletion γ 34.5. R7020 maintained cytolytic activity in the presence of MEK inhibition.

PATIENT SPECIFIC SIMULATED RE-HEARSAL TO ENHANCE THE PLANNING OF ENDOVASCULAR INTERVENTIONS.

Willem Willaert
Ghent University Hospital, Belgium

Introduction: Patient-specific simulated rehearsal of complex endovascular interventions allows incorporation of patient-specific CT data into the simulation software, enabling the interventionalist to evaluate the use of the C-arm, different endovascular tools and the optimal access strategy prior to performing the real procedure on the patient. It is a technological advance for the interventionalist with potential benefits to patients undergoing carotid artery stenting (CAS) procedures.

Objectives: This study aimed to evaluate whether patient-specific rehearsal of a CAS procedure has an influence on the tool selection and the use of fluoroscopy for a complex endovascular procedure such as the CAS intervention. Secondary aims were to evaluate the face validity of this technology and if the potential benefit of patient-specific rehearsal is influenced by the level of CAS experience of the interventionalist.

Materials: Endovascular physicians with a varying degree of CAS experience were recruited and divided into three groups: inexperienced (5-20 CAS), moderately (21-50 CAS) and highly experienced in CAS (>50 CAS procedures). A 3D model was created of an actual patient with the PROCEDURETM rehearsal studio software. Subsequently all participants rehearsed this patient-specific CAS procedure on the AngioMentorTM Express simulator. Pre-operative and postoperative questionnaires registered tool and fluoroscopy preferences in a stepwise fashion for this specific CAS procedure to assess a potential change in material preference. A questionnaire rated face validity, training potential and pre-procedure potential on a Likert scale from 1 (poor) to 5 (excellent).

Methodology: Following case note and CT angiographic review of a real patient case, subjects performed a familiarization virtual iliac procedure. Thereafter they proceeded to the CAS procedure. Endovascular tool requirements, fluoroscopic angles and the face validity were recorded.

Results: Thirty three endovascular physicians with varying degrees of CAS experience participated: inexperienced ($n=11$), moderately ($n=7$) and highly experienced ($n=15$). For all participants 98 of a possible 363 changes (27%) were observed from pre- to post-case questionnaires. This was most notable for optimal fluoroscopy C-arm position 17/33 (52%), chosen guide wire to introduce the sheath in the common carotid artery 15/33 (46%), choice of selective catheter 13/33 (39%) or guiding catheter (or sheath) 12/33 (36%) and balloon dilatation strategy 10/33 (30%). Although modifications in tool preferences were more apparent in the inexperienced group, these alterations were not significantly influenced by level of CAS experience ($p > 0.05$) Face validity of the

model, training potential and pre-procedure potential were rated high by the interventionalists and all measured a median of 4.

Conclusion: Patient-specific simulated rehearsal of a complex endovascular procedure strongly influences tool selection and fluoroscopy. This influence seems irrespective of the prior experience level with CAS. This technology requires further investigation with respect to a potential reduction in the use of endovascular material and X-ray exposition and with respect to improved outcomes in the clinical setting.

COMBINED DISTAL BYPASS AND FREE FLAP FOR CRITICAL LIMB ISCHEMIA WITH EXTENSIVE TISSUE LOSS AND INFECTION

Atsuhiko Koya, Atsuhiko Koya, Nobuyoshi Azuma,
Masashi Inaba, Hisashi Uchida, Taku Kokubo,
Nobuyuki Akasaka, Tadahiro Sasajima
Division of Cardiovascular Surgery, Asahikawa Medical College,
Japan

OBJECTIVE: It is difficult to salvage severe ischemic foot with extensive tissue loss and infection. We reviewed results of combined distal bypass (DB) and free flap (FF), and validated efficacy of the limb salvage operation.

METHODS: During the past 9 years, 293 patients (302 limbs) with ischemic ulcer or gangrene were treated with arterial reconstruction. Of 293 cases, combined DB with autologous graft and FF were performed in 21 patients (22 limbs), whose etiology of peripheral arterial disease was arteriosclerosis in 17, and Burger disease in 4. Eighteen patients had diabetes, 7 were detected ischemic heart disease, and 6 were dialysis-dependent end-staged renal failure (ESRF). Eighteen patients underwent DB to crural or pedal arteries, and 4 patients without graftable distal artery were performed distal venous arterialization. Two cases underwent DB and FF simultaneously, while other cases were received DB first, followed by FF after debridement of necrotic tissue, disinfection, and growing granulation. The types of flap included parascapular cutaneous flap in 8, rectus abdominal flap in 8 and latissimus dorsi flap in 6.

RESULTS: Fourteen flaps were healed primarily, and 2 limbs needed additional FF successfully (72.7%). Two flaps were failed due to inflow graft insufficiency in one Burger disease, and another with microcirculation disorder due to ESRF, and 2 were detached from wound bed because of infection. Only one patient with progressively ischemic change due to severe heart failure was unwillingly received major amputation of bilateral limbs. 2 of six patients with ESRF were died of associated cardiac diseases.

CONCLUSIONS: Combined DB and FF was effective as a last resort of limb salvage technique for patients with extensive tissue

loss. It was suggested selection of candidate, certain graft flow to the flap and disinfection of wound before FF were important for achievement of this therapy

BUERGER DESEASE , a frequent pathology In Orient. Aleppo retrospective study

DR FAYEZ TAMBE
UNIVERSITY OF ALEPPO, Syria

THIS IS A RETROSPECTIVE STUDY CONCERNING 320 PATIENTS OF BUERGER DESEASE ADMITTED BETWEEN 2003 AND 2008 AT THE ALEPPO UNIVERSITY HOSPITAL. BUERGER DESEASE HAS A WORLDWIDE DISTRIBUTION MORE PREVALENT IN THE MIDDLE EAST AND FAR EAST THAN IN THE NORTH AMERICA AND WESTERN EUROPE.

THIS INFLAMMATORY PATHOLOGY AFFECT SMALL AND MILD SIZE VESSEL THAN LARGE VESSELS.

THE USE OF TOBACCO IS CENTRAL TO THE INITIATION AND PROGRESSION OF THE DESEASE.

FOR ALL OUR PATIENTS ,THE CRITERIA OF SELECTION WAS SHINOYA EXCEPT FOR WOMEN WE ADOPT OLLIN CRITERIA.

IN THIS STUDY,WE HAVE AT LESAT 2 YEARS OF OBSERVATION.

THE AIM OF OUR STUDY IS TO DEMONSTRATE THE PREVALENCE OF THIS PATHOLOGY IN NORTH SYRIA

THE SOCIO-ECONOMIC CONDITION OF PEOPLE WITH B.D THE PARTICULARITY OF THE SIGN AND SYMPTOMS IN THE MIDDLE EAST

THE DISASTROUS RESULTS OF ALL KIND OF MEDICAL OR SURGICAL TREATMENT.

THE CENTRAL ROLE OF ABSTINENCE OF TOBACCO IN THE PROGNOSIS.

AND FINALLY WE COMPARE OUR STUDY AT EACH STEP FROM DIAGNOSIS TO TEATMENT AND PROGNOSIS WITH OTHER STUDIES PROVIDING FROM JAPAN ,TURKEY ,EUROPE AND THOSE COMING FROM CLEAVLAND INSTITUTE.

AND WE INDENTIFY SOME SPECIFICITY OF THE DESEASE IN THE MIDDLE EAST CONCERNING SYMPTOMES ,EVOLUTION AND PROGNOSIS

AND THE EFFICACY OF DIFFERENT SURGICAL TREATMENT.

Auto transplantation for renal artery aneurysm in a single kidney;

Mamoun AL-Basheer MBBS (Lond) FRCSI FRCSEd JES
JBVS FICA

Vascular & Endovascular surgeon, King Hussien Centre,
Amman, Jordan
Clinical Fellow, Liver Transplant Surgery, LHSC, London,
Ontario, Canada.

Introduction:

Renal artery aneurysm (RAA) is an infrequently seen disease entity but one with the potential for significant morbidity and mortality.

Symptomatic and large RAAs are more prone to serious complications which mandate proactive management. We report the successful treatment of such an aneurysm in a solitary kidney.

Case report:

We report the case of a 35 year old female who presented with loin pain and was discovered on computed tomographic arteriography with 3-dimensional reconstruction to have a large renal artery aneurysm measuring 5 cm in maximal diameter and involving the bifurcation of the renal artery at the hilum. Five years earlier she had contra lateral nephrectomy at another hospital for non functioning kidney secondary to nephrolithiasis. Following nephrectomy, cold preservation, ex-vivo renal artery aneurysmectomy and renal artery reconstruction, the kidney was transplanted into the left iliac fossa. The internal iliac artery bifurcation was used as the inflow artery connected end to end to both branches of the renal artery. Following an initial period of ATN (acute tubular necrosis) she recovered her renal function back to base line normal renal function and remains well and asymptomatic at 1 year follow up.

Conclusion:

Autotransplantation is a viable option for repair of hilar renal artery aneurysms as it facilitates ex-vivo aneurysmectomy and arterial reconstruction. This case report is further evidence of good outcome even in cases of a single kidney.

Treatment and Prognosis of 27 Cases of Popliteal Artery Aneurysm

Kentaro Kamiya¹, Shunya Shindo¹, Hiroto Uchiyama¹,
Hidenori Inoue¹, Masaaki Cho¹,

Toshiya Nishibe¹, Satoru Shiraiwa², Masahiko
Matsumoto², Hiroshi Shigematsu³,

¹Department of Cardiovascular Surgery, Tokyo Medical
University Hachioji Medical Center, Hachioji-city, Tokyo,
JAPAN

²The 2nd Department of Surgery, Yamanashi University Hospital,
Chuo-city, Yamanashi, JAPAN

³Department of Vascular Surgery, Tokyo Medical University
Hospital, Shinjuku-ku, Tokyo, JAPAN

<Purpose>

Popliteal artery aneurysm (PAA) is the most common peripheral artery aneurysm, comprising 70% to 85% of the total peripheral aneurysms. However, reports have been few in JAPAN. We analyzed 27 cases of PAA experienced at our department to clarify their prognosis.

<Methods>

Six PAAs in 3 patients treated at Tokyo Medical University Hachioji Medical Center from 2009 to 2010 and 21 PAAs in 16 patients treated at Yamanashi University Hospital from 1992 to 2010 were reviewed from their medical records retrospectively.

<Results>

PAAs were diagnosed in 27 legs (Rt: 11, Lt: 16) in 19 patients (Male: 15, Female: 4), ranging from 56 to 93 years of age (mean, 74.3 years). Bilateral PAAs were present in 8 patients (42.1%). Average size of PAA was 33.6 mm (13-70 mm). Six PAAs were treated without operation (22.2%), and 21 PAAs were treated surgically (77.8%). Bypass surgery with exclusion of the aneurysm was performed in 19 legs, using saphenous vein grafts in 7 legs (36.8%), vascular prosthetic grafts in 11 legs (56.7%), and direct anastomosis in 1 leg (5.3%). Below-knee amputations were needed in 2 legs due to gangrene and infection. Acute arterial occlusions were observed in 11 legs (40.7%), of which emergency bypass operations were performed in the 10 legs, while below-knee amputation was performed in the remaining case. Complications with nerve dysfunction after emergency operation were experienced in 6 legs. Coexisting aneurysms with PAA were identified in 9 patients (47.4%); abdominal aortic aneurysms in 4 patients, common iliac arterial aneurysms in 2 patients, and femoral arterial aneurysms in 5 patients.

<Conclusions>

PAA is not yet a popular disease in JAPAN. We must increase the recognition of the disease, leading to more appropriate treatment for limb salvage. Multiple aneurysms should be cared immediately.

Does "on-site" vascular surgery improve ruptured abdominal aortic aneurysm survival?

Danny Chiu

MONASH UNIVERSITY, EASTERN HEALTH, Australia

Eastern Health encompasses three major emergency departments but only one is linked to an "on-site" vascular surgical service. Ruptured abdominal aortic aneurysms, presenting at the other two sites need to be transferred for intervention.

Between 2002 and 2008, 101 patients were identified. 68 patients presented to the hospital with on-site vascular services (on-site group) and 33 patients presented to other sites without vascular services and potentially needed to be transferred for intervention (transfer group).

The average age and male predominance in these two groups were not statistically different. The decision not to operate was made in 29% for the on-site group and 33% for the transfer group. All of these patients died.

The operative mortality was 33% and 34% and the overall mortality was 54% and 55% for the "on-site" and transfer group respectively. The average total length of stay and time in ICU of both groups were not statistically different.

Despite the same patients outcomes, the time to operation (time from ED presentation to operation commencement) between these two groups was significantly different. (median time "on-site" group 92 minutes, "transfer" group 240 minutes, $p < 0.01$).

These results indicate that the significant difference in time to operation between these two groups did not influence patient outcome, nor did the lack of on-site vascular surgical service lead to selective intervention. The development of vascular services at each site is not warranted for the purpose of treating ruptured abdominal aortic aneurysms.

It is not possible to extrapolate these results to situations where longer transfer times are applied but further studies are warranted.

lished. The potential loss of patient fitness during surveillance of small AAAs may preclude timely repair, particularly for those patients unsuitable for endovascular aneurysm repair (EVAR). The purpose of this study was to assess the longitudinal changes in patient fitness and EVAR suitability during surveillance of small AAAs and their potential implications for management.

Methods: We studied 62 patients referred for evaluation of nonruptured small AAAs who underwent follow-up by CT angiography. Morphologic aortic aneurysm features and EVAR suitability were measured according to SVS reporting standards. Fitness for surgical repair was assessed using the Customized Probability Index, a validated fitness score for AAA repair. Changes in patient fitness and EVAR suitability were assessed using paired nonparametric and survival analyses.

Results: The median age of the study cohort was 74 years (interquartile range [IQR], 65-77 years). The initial median fitness score was +4 (IQR, -5, +9). The median follow-up duration was 36 months (IQR, 16-53 months). Overall, patient fitness for open repair significantly decreased during the study period (63% vs 43% considered fit for open repair; McNemar test, $P < .001$). In fact, the median fitness score increased from +4 to +8.5 ($P = .001$). The anatomic suitability for EVAR also significantly changed (81% vs 69%; $P < .001$). Of note, 45% of AAAs with marginal neck morphology, i.e. length < 15 mm and diameter > 28 mm, vs. 3% of those with adequate necks were not suitable for EVAR at the end of follow-up ($P < .001$). Long-term patient survival was not affected by patient fitness. Survival rates at 1, 3 and 5 years were 95%, 87% and 70% for unfit patients vs. 96%, 92% and 73% for fit patients, respectively ($P = 0.8$).

Conclusions: Significant changes in patient fitness and EVAR suitability occur during surveillance of small AAAs. EVAR suitability is primarily lost in small AAAs with marginal neck morphology. These data indicate that early repair for small AAAs may be justified in patients fit for open repair if they are unsuitable for EVAR or have marginal necks for EVAR, since surveillance may result in loss of patient fitness and/or EVAR suitability that may preclude future repair.

Changes In Patient Fitness And EVAR Suitability During Surveillance Of Small AAAs: Which Should Have Early Repair?

Carlos Timaran, Andres E Martinez, Eric B Rosero,

Adriana Ilarraza, J Gregory Modrall, G Patrick Clagett

Univ of Texas Southwestern Medical Center, Dallas, TX, USA

Purpose: The need for treatment of abdominal aortic aneurysms (AAAs) in patients unfit for open repair has not been estab-

RANDOMISED CONTROLLED TRIAL OF TREATMENT OF INTERMITTENT CLAUDICATION DUE TO INFRA INGUINAL ATHEROSCLEROTIC DISEASE

Fayyaz Ali Khan Mazari, Junaid Khan, MNA Abdul Rahman, Katherine Mockford, Sumit Gulati, HLD Lee, Tapan Mehta, Peter T McCollum, Ian C Chetter.
Alderson House Hull Royal Infirmary, Alderson House Hull Royal Infirmary, United Kingdom

OBJECTIVES:

To compare the clinical, quality of life (QOL) and economic outcomes for percutaneous transluminal angioplasty (PTA), supervised exercise programme (SEP) and combined therapy (PTA+SEP) in the treatment of intermittent claudication (IC) due to femoro-popliteal atherosclerotic disease.

METHODS:

Patients with femoro-popliteal IC were randomised to receive PTA, SEP or PTA+SEP. Patients with critical limb ischaemia were excluded. All patients received best medical treatment including anti-platelet medication, lipid lowering drugs, smoking cessation advice and risk factor modification. Assessments were performed prior to and at 1, 3, 6 and 12 months post intervention. Clinical outcomes (pre & post exercise ankle brachial pressure index, treadmill intermittent claudication distance & maximum walking distance, patient reported walking distance, ISCVS outcomes) and quality of life indicators (generic SF36 and disease specific VascuQoL) were recorded at each visit. SF-6D health utility index was calculated from SF-36 and plotted for all time points. Quality Adjusted Life Years (QALYs) were generated by calculating area under the curve. Costs were calculated using National Health Service 2009-10 payment by results tariffs (NHS-PBR), National Institute of Health Research Clinical Research Network investigation pricing index and BUPA Healthcare pricelists. Adjustments to treatment costs were made for re-interventions. Cost per QALY and incremental costs were calculated for each procedure. Multiple sensitivity analyses were performed for variation in utility and cost calculations to check robustness of results.

RESULTS:

Over a 6 year period 178 patients were recruited and randomised to the three treatment arms (PTA 60, SEP 60, PTA+SEP 58). All groups were well matched at baseline for demographics, co-morbidities and TASC grading. 34 patients withdrew from the trial or were lost to follow up.

Clinical & QOL Outcomes:

Intra group analysis:

All groups demonstrated significant clinical and QOL improvements (Friedman test, $p < 0.05$).

SEP (60 patients, 14 withdrew) 69.6% of patients ($n=32$) improved following treatment [19mild, 10moderate, 3marked], 13% ($n=6$) no improvement and 17.4% ($n=8$) deteriorated. 8.3% ($n=5$) of

patients required re-intervention within 1 year (4 PTA, 1 Femoro-popliteal bypass).

PTA (60 patients, 8 withdrew) 71.1% of patients ($n=37$) improved following treatment [16 mild, 16 moderate, 5 marked], 17.3% ($n=9$) no improvement and 11.6% ($n=6$) deteriorated. 13.3% ($n=8$) of patients required re-intervention within 1 year (7 PTA, 1 femoro-popliteal bypass).

PTA+SEP (58 patients, 12 withdrew) 87.0% of patients ($n=40$) improved following treatment. [18mild, 20moderate, 2marked], 13.0% ($n=6$) no improvement and 0% ($n=0$) deteriorated. No patient required re-intervention within 1 year.

Inter group Analysis:

PTA & SEP were equally effective in improving clinical outcome significantly, however, the effect was short lived. PTA+SEP produce a sustained improvement in clinical outcome measures than PTA or SEP alone, but there was no significant QOL advantage (Kruskal Wallis test, $p > 0.05$).

Economic Outcomes:

Intra group analysis:

All treatments resulted in statistically significant improvement in SF-6D index score (Friedman test, $p < 0.05$).

Inter group analysis:

QALYs: There was no significant difference (ANOVA, $p > 0.05$) between treatments in mean QALYs gained [PTA 0.620 (95%CI 0.588-0.652), SEP 0.629 (95%CI 0.597-0.660) PTA+SEP 0.649 (95%CI 0.622-0.675)].

COSTS: Primary unadjusted cost per procedure was £5,492.75 for PTA, £2,832.74 for SEP and £5,830.74 for PTA+SEP. After adjustment for re-interventions (PTA 8, SEP 5, PTA+SEP 0), mean cost per procedure was significantly higher (ANOVA, $p > 0.05$) for PTA (£6,049.23) compared to SEP (£3,198.13) and PTA+SEP (£5,830.74). Consequently, cost per QALY was significantly higher for PTA (£9,756.82) compared to SEP (£5,084.47) and PTA+SEP (£8,984.19). This resulted in an incremental cost of £26,642.41 if PTA was used alone compared to PTA+SEP; and £519,150.00 if PTA was used instead of SEP to equate the QALY gain achieved by these treatments.

These results were robust and valid in all sensitivity analyses.

CONCLUSIONS:

PTA, SEP & combined therapy (PTA+SEP) are effective treatments for femoro-popliteal atherosclerotic disease. Combined therapy (PTA+SEP) produces sustained results compared to either treatment alone. SEP is the most cost effective and should be the first line treatment for IC in this patient group. Combined therapy is more cost effective than PTA alone and should be provided as standard treatment where applicable. Provision of SEP in community can result in further reduction of costs and improve patient compliance and satisfaction.

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Review Article

Current Reconstructive Techniques Following Head and Neck Cancer Resection Using Microvascular Surgery

Takeharu Kanazawa, MD, PhD,¹ Shunji Sarukawa,² Hirofumi Fukushima,³ Shoji Takeoda,⁴ Gen Kusaka,⁵ and Keiichi Ichimura¹

Various techniques have been developed to reconstruct head and neck defects following surgery to restore function and cosmetics. Free tissue transfer using microvascular anastomosis has transformed surgical outcomes and the quality of life for head and neck cancer patients because this technique has made it possible for surgeons to perform more aggressive ablative surgery, but there is room for improvement to achieve a satisfactory survival rate. Reconstruction using the free tissue transfer technique is closely related to cardiovascular surgery because the anastomosis techniques used by head and neck surgeons are based on those of cardiovascular surgeons; thus, suggestions from cardiovascular surgeons might lead to further development of this field. The aim of this article is to present the recent general concepts of reconstruction procedures and our experiences of reconstructive surgeries of the oral cavity, mandible, maxilla, oropharynx and hypopharynx to help cardiovascular surgeons understand the reconstructions and share knowledge among themselves and with neck surgeons to develop future directions in head and neck reconstruction.

Key words: free tissue transfer, microvascular anastomosis, head and neck reconstruction

INTRODUCTION

Head and neck cancer refers to a group of biologically similar cancers originating from the oral cavity, nasal cavity, paranasal sinuses, pharynx and larynx. Most

head and neck cancers are squamous cell carcinomas (HNSCC), originating from the epithelium of these regions. HNSCC are frequently aggressive in their biologic behavior, and many patients have advanced disease. With recent advances in concurrent chemoradiotherapy (CCRT), organ conservation is an important aim in HNSCC therapy,¹⁾ similar to disease control; however, CCRT is limited to the control rate of advanced local cancer, and post-therapeutic dysfunction is still an issue.^{2,3)} More than 50% of advanced HNSCCs require reconstruction of surgical defects to prevent functional and cosmetic issues (our original data). Furthermore, as there are many important structures in the head and neck region, complications after surgery sometimes result in postoperative death by rupture of the carotid artery and meningitis after skull base surgery. Thus, life-saving is also an important goal of head and neck reconstruction. The head and neck region is one of the most difficult areas to reconstruct because it has complex anatomic, functional and physiologic interactions. Thus, many reconstructive techniques for surgical defects have been developed.

¹Department of Otolaryngology / Head and Neck Surgery, Jichi Medical University School of Medicine, Shimotsuke, Tochigi, Japan

²Department of Plastic and Reconstructive Surgery, Jichi Medical University School of Medicine, Shimotsuke, Tochigi, Japan

³Department of Head and Neck, Cancer Institute Hospital, Japanese Foundation for Cancer Research, Tokyo, Japan

⁴Department of Otolaryngology, Hasuda Hospital, Hasuda, Saitama, Japan

⁵Department of Neurosurgery, Jichi Medical University Saitama Medical Center, Saitama, Saitama, Japan

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Corresponding author: Takeharu Kanazawa, MD, PhD. Department of Otolaryngology, Head and Neck Surgery, Jichi Medical University, School of Medicine, 3311-1 Yakushiji, Shimotsuke, Tochigi 329-0498, Japan

Tel: +81-285-58-7381, Fax: +81-285-44-5547

E-mail: kanatake@omiya.jichi.ac.jp

Previously, pedicled flaps and alloplasts were commonly used to reconstruct the head and neck region.^{4,5)} Pedicled flaps, such as the pectoralis major, latissimus dorsi and trapezius, still play an important role in reconstruction of large defects,⁵⁻⁷⁾ but they may yield unsatisfactory functional and cosmetic results because of donor site morbidity and limitations relating to bulk.⁸⁾ Head and neck reconstruction using microvascular surgery was first reported by Seidenberg in 1959,⁹⁾ and Daniel et al. reported the advanced technique of microvascular anastomosis using a dedicated microscope in 1973.¹⁰⁾

Recent progress in vascular surgery techniques has made it possible to develop head and neck reconstruction using free tissue transfer for defects after surgical resection.^{11, 12)} The advantages of free tissue transfer are to avoid the limitations of pedicle length and also to enable selection of the most appropriate tissue to replace surgical defects. At present, free tissue transfer is the standard approach for head and neck reconstruction.^{8, 13, 14)} Reconstruction using the free tissue transfer technique is closely related to cardiovascular surgery because the anastomosis techniques used by head and neck surgeons are based on those of cardiovascular surgeons. As a few head and neck surgeons are sufficiently skilled in microvascular anastomoses, free tissue transfer for head and neck reconstruction is performed in limited institutions. If cardiovascular surgeons could master free tissue transfers, head and neck reconstruction using free tissue transfer would be a common procedure that could be performed in many institutions. The aim of this article is to present recent head and neck reconstruction procedures and our experiences to help develop an understanding by cardiovascular surgeons, and to share knowledge with both head and neck surgeons and cardiovascular surgeons to discuss future directions in head and neck reconstruction.

MICROVASCULAR ANASTOMOSES

Free tissue transfer permits the transfer of suitable distant tissue to the recipient site by means of microvascular anastomoses. As it has its own arterial supply and venous drainage system, the transferred tissue can provide a good blood supply. Microvascular anastomoses are indispensable techniques for head and neck reconstruction using free tissue transfer. With the development of improved optic microscopes and fine instruments and devices for microsurgery, the patency rates of anastomosed vessels have reached more than 90% and consequently, flap survival has become the norm.¹²⁾ In general,

microvascular anastomoses are performed by conventional hand suturing.^{12, 15)} Under microscopic vision, the vessel ends of the donor site are freshened by recutting the edges and removing the adventitia 2 mm from the ends, and then the vessels are anastomosed with 9-0 or 10-0 nylon combined knotting with running microsutures to the artery and vein on the recipient side. Although the conventional method is used as the standard, anastomotic coupling devices are becoming acceptable.¹⁶⁾ The common arteries used as donor vessels are the superior thyroid artery, the main trunk of the external carotid artery, the transverse cervical artery and the facial artery. The most common vein used as the recipient vessel is the internal jugular vein (end-to-side anastomosis).¹⁷⁾ Among postoperative complications in free flap transfer, total flap necrosis caused by vascular thrombosis in particular is extremely serious, and the rate of total flap necrosis ranges from 0.8% to 7.7%.^{12, 18)} Many factors, such as patient age, tobacco use, systemic disease, obesity, a protracted surgical time, an interposition vein graft and prior radiation exposure, have been previously reported being associated with flap necrosis^{19, 20)}; however, a recent study demonstrated that the only significant risk factor for total flap necrosis was a history of CCRT,¹⁷⁾ and another report showed that diabetes mellitus increased the failure rate.¹⁵⁾ Although significant factors in flap failure are not yet clear, we suggest that surgeons should take into consideration the preceding general condition, the suturing technique and the selection of the flap for patients with candidate risk factors.

ORAL CAVITY

In the oral cavity, the most common site of cancer is the tongue, followed by the floor of the mouth, cheek lining, gingiva, lips and palate.

Surgery in this area inevitably disturbs function because it removes the intrinsic pedicle muscles of the tongue to a greater extent, including major sensory and motor nerves, leading to neurological deficits, and leaves a tongue remnant of variable size and loss of mucosa from the floor of the mouth. The two contrasting views are whether it is better to fully replace the lost tissue and fill the whole dead space or to just restore oral tongue continuity by minimal replacement of soft tissue.¹⁴⁾

Surgeons advocating full reconstruction of the lost tissue are likely to use a thick flap, such as a latissimus dorsi or rectus abdominis flap, because they believe full reconstruction is necessary for static oral phase swallowing.^{14, 21)}

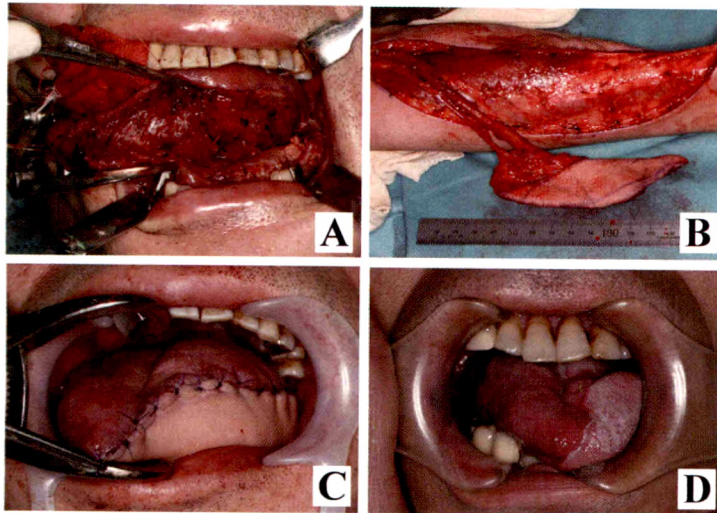


Fig. 1 Reconstruction of the tongue using radical forearm flap. **A:** Surgical defect of the tongue. **B:** Radical forearm flap. **C:** Reconstruction of the tongue. **D:** One year after reconstruction.

On the other hand, those who advocate reconstruction with minimal soft tissue replacement to maintain function as dynamic reconstruction commonly use a radial forearm flap, as the residual tongue tissue undergoes hypertrophy following reconstruction providing that the tongue remnant is maintained in the correct anatomical position.^{14, 22)} In our opinion, no one type of flap is significantly superior with respect to functional outcome. The type of flap reconstruction is determined mainly by the expected size of the defect. The radical forearm flap is the first choice for reconstruction because of its thin and pliable nature (**Fig. 1**). Free myocutaneous flaps, such as a free rectus abdominis flap, are needed for larger volume defects. Suturing a flap to the surgical margin to maintain the mobility of the remaining structure is important in patients with a relatively small defect after resection. For larger defects, the type of flap should be determined individually in consideration of a variety of factors, including defect volume at the recipient site, the skill of the surgeon and donor site morbidity. Furthermore, re-innervated free tissue transfer may not be mandatory, and we do not perform the re-innervation of either sensory or motor nerves.

CARCINOMA INVOLVING THE MANDIBLE

Cancer involving the mandible is usually secondary to direct extension from the oral cavity or the oropharynx. Surgical management usually requires either partial horizontal resection or segmental resection. The length of the resection is dependent on the extent of the tumor and resected portions of mandible, such as the posterior vertical, the lateral, the anterior, or a combination of these

resections. In addition to bone resection, a varying volume of soft tissue is inevitably resected. Thus, several combined flaps are used for mandible reconstruction, such as a fibular flap, scapular flap and deep circumflex iliac flap.^{23–26)} The fibular flap and scapular flap are commonly used for mandible reconstruction.²⁷⁾ The scapular flap, meaning the flap vascularized by the chimeric nature of the subscapular vascular system, allows harvest of multiple, independent skin paddles, serratus muscle/rib, latissimus dorsi muscle and up to 12 cm of lateral scapular bone.^{24, 26)}

These features make it the ideal flap for complex composite defects with large soft tissue requirements, such as mandibular continuity defects with simultaneous intraoral and extraoral components.²⁴⁾ The disadvantages of the traditional scapular flap include a short vascular pedicle, inadequate bone quantity and reliable support of osseointegrated dental implants, and need for intraoperative position changes.^{24, 26)} The fibular flap has excellent bone quality and quantity, up to 25 cm, of sufficient pedicle length.^{23, 26, 27)} Furthermore, the complication rates and donor site morbidity have generally been acceptable. The disadvantages of the flap are its associated skin paddle, which is of somewhat limited size and flexibility,^{23, 26)} and the limited bone height availability of the osseointegrated implant flap.²⁶⁾

Although a report has described that the fibular flap is the best work horse,²³⁾ we usually use the scapular flap to reconstruct the mandible because of its advantages (**Fig. 2**). If more than 12 cm bone length is required, we use a fibular flap, but sometimes combine it with other flaps, such as a radial forearm flap to fill soft-tissue defects. The deep circumflex iliac artery (DCIA) flap, which offers a

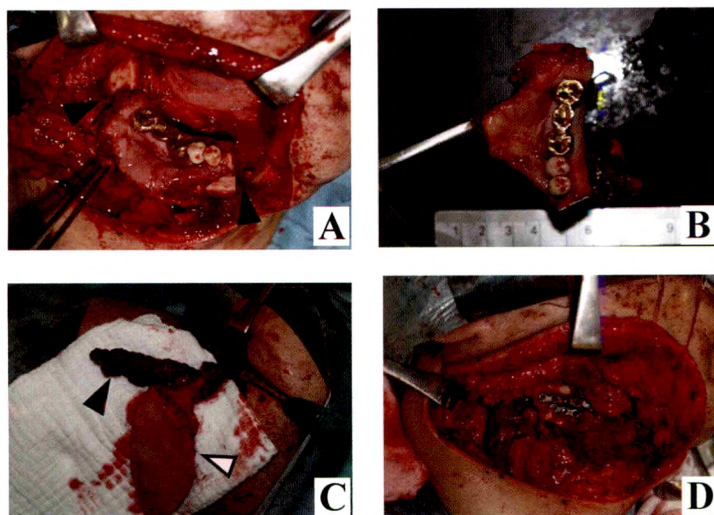


Fig. 2 Reconstruction of the mandible using a scapular flap. **A:** Segmental resection of the mandible. The portion between arrowheads was resected. **B:** Specimen following the resection of invasive squamous cell carcinoma of the right gum. **C:** Scapular flap based on the subscapular artery, showing the latissimus dorsi with the thoracodorsal artery (open arrowhead) and the scapula portion of the flap with circumflex scapular artery (closed arrowhead). **D:** Reconstruction of mandible using scapular flap.

large amount of abundant bone that can be shaped like a hemi-mandible, is also reportedly ideal for mandibular reconstruction, particularly when osseointegrated implants are being considered.^{24, 26)} This is used when bulky bone is required and there is a relatively small soft-tissue defect, but it is not so common.

MAXILLA

Reconstruction after total maxillectomy may involve various soft tissues with or without bony requirements, which are determined by the extent of the resection. Many of these defects result in significant functional and aesthetic sequelae. These may include collapse of the lip, cheek and infraorbital soft tissues, orbital complication, and loss of the hemi-palate, leading to a compromised oral phase of swallowing and difficulty with speech articulation.

Total maxillectomy defects are challenging from both a functional and aesthetic perspective. These defects result in loss of a significant amount of bone and sometimes soft tissue of the cheek. The two contrasting views are whether a bone-containing flap or myocutaneous flap with a free bone graft is needed for maxilla reconstruction.^{28, 29)}

Surgeons who advocate bone-containing flaps frequently used the scapula-latissimus osteomyocutaneous flap, including the thoracodorsal arterial system to reconstruct the orbital floor and/or anterior arch.³⁰⁾ This flap is considered applicable to various defects of the maxilla, because each of the reconstruction materials can be used flexibly.

Surgeons who advocate a myocutaneous flap with a

free bone graft carefully use a rectus abdominis flap with a cranial bone graft, rectus abdominis fascia, costal cartilage or titanium mesh implants to restore the orbital floor and/or anterior arch.^{31, 32)} Conflicting results have been reported about reconstruction after total maxillectomy using a rectus abdominis flap. Muneuchi et al. noted that the rectus abdominis flap, even when harvested with costal cartilage, provides only minimum suspension for the prevention of orbital floor prolapse and is insufficient for bony reconstruction.³¹⁾ An important advantage of the rectus abdominis flap is that it can be harvested simultaneously with a maxillectomy in the supine position.³¹⁾ On the other hand, the same studies indicated that a vascularized bone graft is not necessary, and used a rectus abdominis flap because there is enough muscle volume to cover alloplastic implants (titanium mesh) and a large volume of adipose tissue required for most maxillary reconstructions,³²⁾ leading to the use of titanium mesh to avoid the need for bone grafting, and may be especially beneficial in fragile or aged patients.

In our opinion, the choice of flap depends on the remaining zygomatic bone. As most patients have enough zygomatic bone remaining to prevent prolapse of the orbital floor, we usually use a rectus abdominis flap with costal cartilage (**Fig. 3**) or titanium mesh. If the zygomatic bone is completely resected, bone-containing flaps should be used, but this is relatively rare.

OROPHARYNX

The oropharynx is the middle part of the throat, which includes the base of the tongue, tonsils, soft palate, and the posterior wall of the pharynx. Larger defects after

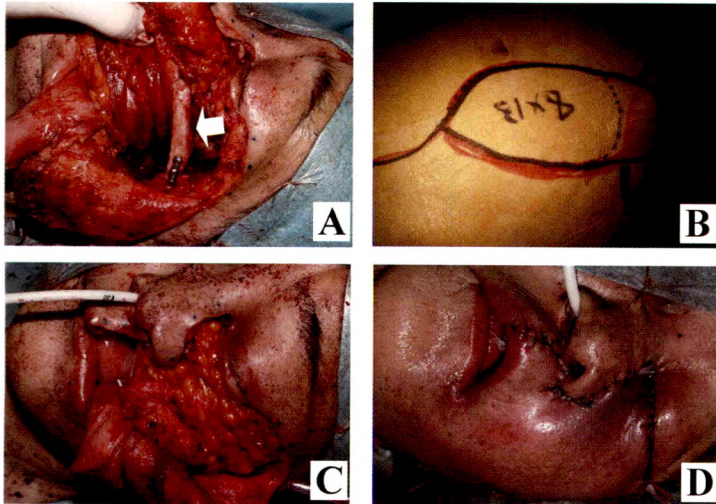


Fig. 3 Reconstruction after total maxillectomy. **A:** Costal cartilage (arrowhead) used to reconstruct the orbital rim and orbital floor. **B:** Design of the rectus abdominis free flap. **C:** Rectus abdominis free flap filling the maxillectomy defect to cover the costal cartilage and restore the oral palate. **D:** Postoperative result.

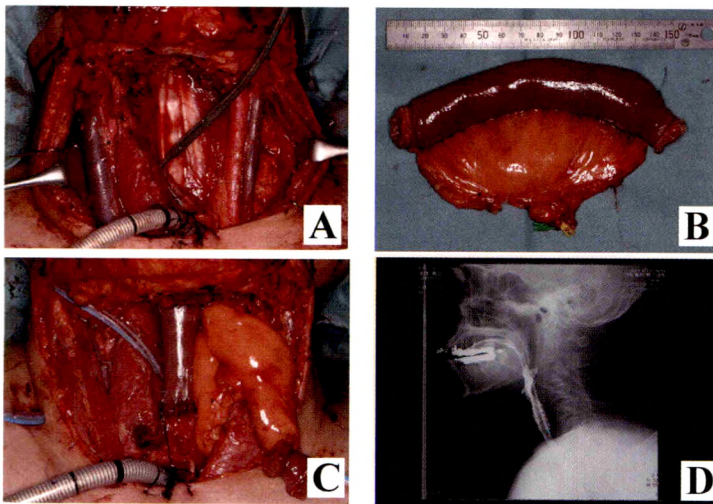


Fig. 4 Reconstruction after pharyngolaryngoesophagectomy. **A:** Surgical defect after pharyngolaryngoesophagectomy. **B:** Free jejunal flap. **C:** Reconstruction of pharynx and cervical esophagus. **D:** Pharyngo-esophagogram is usually performed to confirm a complete reconstruction.

oropharyngeal resection, such as total palatal, more than 50% of the tongue base, and composite tongue base/palatal/pharyngeal defects may be closed with a radical forearm and anterolateral thigh flap free flap, and rectus abdominis flap, as an alternative to regional myocutaneous pedicled flaps. Free gastro-omental flaps may also be used for oropharyngeal reconstruction. The fibular flaps are an excellent option for defects involving bone. The scapular free flap may also be used, and offers the advantage of having two skin paddles (scapular and parascapular) for internal and external lining.^{33, 34)}

HYPOPHARYNX

Hypopharyngeal cancers are regarded as relatively rare, but are now increasing in number. They have poor survival rates compared with cancers at other head and

neck sites. Multimodal treatment is the norm and most surgeries are performed as a pharyngolaryngoesophagectomy.³⁵⁾ If it is necessary to carry out a pharyngolaryngoesophagectomy, the patient is left with a massive functional defect, which grossly compromises both speech and swallowing. The reconstructive surgeon attempts to restore functional continuity for swallowing and at the same time enable a conduit for esophageal speech. Free jejunal flap transfer is the standard technique for reconstruction after pharyngolaryngoesophagectomy in Japan (Fig. 4)³⁶⁾ because this flap has many advantages, such as a low rate of leakage and stenosis. Jejuna also have a large and adequate vasculature, enabling freedom to select mesenteric vessels and a greater range of safety margin for tumor resection by harvesting a sufficient length of intestinal segment.^{36, 37)} Furthermore, an anastomotic procedure after harvest shows little impact on the

digestive system, with a low rate of surgical complications. Thus, the goal of the free jejunum graft is a single stage reconstruction with a low complication rate, such as leakage and stenosis, short hospital stay and early restoration of swallowing.

Reports from other countries indicated that free fasciocutaneous tubed flaps, such as a radical forearm flap or anterolateral thigh flap, have several advantages. A recent comparative study indicated that an anterolateral thigh flap results in better speech (fluent tracheoesophageal speech in 89% vs. 22%), swallowing function (oral intake in 95% vs. 65%), and quicker recovery, and is more cost-effective than the jejunal flap for pharyngoesophageal reconstruction.^{13, 38)} Thus, fasciocutaneous tubed flaps should be considered in Japan.

CONCLUSION

We have reviewed head and neck reconstruction surgery and presented typical cases of HNSCC requiring reconstruction after resection to help the understanding of cardiovascular surgeons. Free tissue transfer with microvascular surgery has become the standard of care and has transformed surgical outcomes and the quality of life of patients who undergo major ablative surgery. Such a development has been enabled by the progression of vascular surgery techniques. Free tissue transfer using microvascular surgery is considered to be the most important breakthrough in this field in the last century; however, even aggressive surgeries including free tissue transfer cannot achieve a satisfactory survival rate over the long term. Recently, novel techniques such as in situ tissue engineering have been used clinically. For instance, Iino et al. reported 15 mandibular reconstructions using the Dumbach Titan Mesh-System and particulate cancellous bone and marrow.³⁹⁾ Refinement of the current techniques and development of novel techniques should continue to improve the outcome and quality of life in this challenging patient population.

REFERENCES

- 1) Pignon JP, Bourhis J, Domenge C, et al. Chemotherapy added to locoregional treatment for head and neck squamous-cell carcinoma: three meta-analyses of updated individual data. MACH-NC Collaborative Group. Meta-Analysis of Chemotherapy on Head and Neck Cancer. *Lancet* 2000; **355**: 949-55.
- 2) El-Deiry M, Funk GF, Nalwa S, et al. Long-term quality of life for surgical and nonsurgical treatment of

- head and neck cancer. *Arch Otolaryngol Head Neck Surg* 2005; **131**: 879-5.
- 3) Mowry SE, Ho A, Lotempio MM, et al. Quality of life in advanced oropharyngeal carcinoma after chemoradiation versus surgery and radiation. *Laryngoscope* 2006; **116**: 1589-93.
- 4) Robb GL, Marunick MT, Martin JW, et al. Midface reconstruction: surgical reconstruction versus prosthesis. *Head Neck* 2001; **23**: 48-58.
- 5) Ariyan S. The pectoralis major myocutaneous flap. A versatile flap for reconstruction in the head and neck. *Plast Reconstr Surg* 1979; **63**: 73-81.
- 6) Prakash PJ, Gupta AK. The subscapular approach in head and neck reconstruction with the pedicled latissimus dorsi myocutaneous flap. *Br J Plast Surg* 2001; **54**: 680-3.
- 7) Chen WL, Zhang DM, Yang ZH, et al. Extended supraclavicular fasciocutaneous island flap based on the transverse cervical artery for head and neck reconstruction after cancer ablation. *J Oral Maxillofac Surg* 2010; **68**: 2422-30.
- 8) Futran ND, Mendez E. Developments in reconstruction of midface and maxilla. *Lancet Oncol* 2006; **7**: 249-58.
- 9) Seidenberg B, Rosenak SS, Hurwitt ES, et al. Immediate reconstruction of the cervical esophagus by a revascularized isolated jejunal segment. *Ann Surg* 1959; **149**: 162-71.
- 10) Daniel RK, Taylor GI. Distant transfer of an island flap by microvascular anastomoses. A clinical technique. *Plast Reconstr Surg* 1973; **52**: 111-7.
- 11) Harii K, Ohmori K, Torii S, et al. Microvascular free skin flap transfer. *Clin Plast Surg* 1978; **5**: 239-63.
- 12) Nakatsuka T, Harii K, Asato H, et al. Analytic review of 2372 free flap transfers for head and neck reconstruction following cancer resection. *J Reconstr Microsurg* 2003; **19**: 363-8.
- 13) de Bree R, Rinaldo A, Genden EM, et al. Modern reconstruction techniques for oral and pharyngeal defects after tumor resection. *Eur Arch Otorhinolaryngol* 2008; **265**: 1-9.
- 14) Vaughan ED. Functional outcomes of free tissue transfer in head and neck cancer reconstruction. *Oral Oncol* 2009; **45**: 421-30.
- 15) Joo YH, Sun DI, Park JO, et al. Risk factors of free flap compromise in 247 cases of microvascular head and neck reconstruction: a single surgeon's experience. *Eur Arch Otorhinolaryngol* 2010; **267**: 1629-33.
- 16) Barker EV, Enepekides DJ. The utility of microvascular anastomotic devices in head and neck reconstruction. *Curr Opin Otolaryngol Head Neck Surg* 2008; **16**: 331-4.
- 17) Yoshimoto S, Kawabata K, Mitani H. Factors involved in free flap thrombosis after reconstructive surgery for head and neck cancer. *Auris Nasus Larynx* 2010; **37**: 212-6.
- 18) Yoshimoto S, Kawabata K, Mitani H. Analysis of 59 cases with free flap thrombosis after reconstructive

- surgery for head and neck cancer. *Auris Nasus Larynx* 2010; **37**: 205-11.
- 19) Khouri RK, Cooley BC, Kunselman AR, et al. A prospective study of microvascular free-flap surgery and outcome. *Plast Reconstr Surg* 1998; **102**: 711-21.
 - 20) Eckardt A, Fokas K. Microsurgical reconstruction in the head and neck region: an 18-year experience with 500 consecutive cases. *J Craniomaxillofac Surg* 2003; **31**: 197-201.
 - 21) Yun IS, Lee DW, Lee WJ, et al. Correlation of neotongue volume changes with functional outcomes after long-term follow-up of total glossectomy. *J Craniofac Surg* 2010; **21**: 111-6.
 - 22) Brown L, Rieger JM, Harris J, et al. A longitudinal study of functional outcomes after surgical resection and microvascular reconstruction for oral cancer: tongue mobility and swallowing function. *J Oral Maxillofac Surg* 2010; **68**: 2690-700.
 - 23) Smolka K, Kraehenbuehl M, Eggensperger N, et al. Fibula free flap reconstruction of the mandible in cancer patients: evaluation of a combined surgical and prosthodontic treatment concept. *Oral Oncol* 2008; **44**: 571-81.
 - 24) Valentini V, Gennaro P, Torroni A, et al. Scapula free flap for complex maxillofacial reconstruction. *J Craniofac Surg* 2009; **20**: 1125-31.
 - 25) Yilmaz M, Vayvada H, Menderes A, et al. A comparison of vascularized fibular flap and iliac crest flap for mandibular reconstruction. *J Craniofac Surg* 2008; **19**: 227-34.
 - 26) Miles BA, Goldstein DP, Gilbert RW, et al. Mandible reconstruction. *Curr Opin Otolaryngol Head Neck Surg* 2010; **18**: 317-22.
 - 27) Militsakh ON, Werle A, Mohyuddin N, et al. Comparison of radial forearm with fibula and scapula osteocutaneous free flaps for oromandibular reconstruction. *Arch Otolaryngol Head Neck Surg* 2005; **131**: 571-5.
 - 28) O'Connell DA, Futran ND. Reconstruction of the midface and maxilla. *Curr Opin Otolaryngol Head Neck Surg* 2010; **18**: 304-10.
 - 29) Triana RJ Jr, Uglesic V, Virag M, et al. Microvascular free flap reconstructive options in patients with partial and total maxillectomy defects. *Arch Facial Plast Surg* 2000; **2**: 91-101.
 - 30) Granick MS, Ramasastry SS, Newton ED, et al. Reconstruction of complex maxillectomy defects with the scapular-free flap. *Head Neck* 1990; **12**: 377-85.
 - 31) Muneuchi G, Miyabe K, Hoshikawa H, et al. Postoperative complications and long-term prognosis of microsurgical reconstruction after total maxillectomy. *Microsurgery* 2006; **26**: 171-6.
 - 32) Sarukawa S, Sakuraba M, Asano T, et al. Immediate maxillary reconstruction after malignant tumor extirpation. *Eur J Surg Oncol* 2007; **33**: 518-23.
 - 33) Sabri A. Oropharyngeal reconstruction: current state of the art. *Curr Opin Otolaryngol Head Neck Surg* 2003; **11**: 251-4.
 - 34) Wong CH, Wei FC. Microsurgical free flap in head and neck reconstruction. *Head Neck* 2010; **32**: 1236-45.
 - 35) Kadota H, Fukushima J, Nakashima T, et al. Comparison of salvage and planned pharyngolaryngectomy with jejunal transfer for hypopharyngeal carcinoma after chemoradiotherapy. *Laryngoscope* 2010; **120**: 1103-8.
 - 36) Nakatsuka T, Harii K, Asato H, et al. Comparative evaluation in pharyngo-oesophageal reconstruction: radial forearm flap compared with jejunal flap. A 10-year experience. *Scand J Plast Reconstr Surg Hand Surg* 1998; **32**: 307-10.
 - 37) Zhao D, Gao X, Guan L, et al. Free jejunal graft for reconstruction of defects in the hypopharynx and cervical esophagus following the cancer resections. *J Gastrointest Surg* 2009; **13**: 1368-72.
 - 38) Yu P, Lewin JS, Reece GP, et al. Comparison of clinical and functional outcomes and hospital costs following pharyngoesophageal reconstruction with the anterolateral thigh free flap versus the jejunal flap. *Plast Reconstr Surg* 2006; **117**: 968-74.
 - 39) Iino M, Fukuda M, Nagai H, et al. Evaluation of 15 mandibular reconstructions with Dumbach Titan Mesh-System and particulate cancellous bone and marrow harvested from bilateral posterior ilia. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2009; **107**: e1-8.

» Original Article «

Enhanced Neovascular Formation in a Novel Hydrogel Matrix Consisting of Citric Acid and Collagen

Mikiko Nagayoshi, MD,^{1,2} Tetsushi Taguchi, PhD,³ Hiroyuki Koyama, MD,^{1,2} Tsuyoshi Takato, MD,² Tetsuro Miyata, MD,¹ and Hirokazu Nagawa, MD¹

Background: Three-dimensional regenerative tissue with large bulk generally requires blood perfusion through a vascular network to maintain its viability, and one promising approach is induction of neovascular growth from the recipient bed into the tissue. To induce ingrowth of a vascular network, it is necessary to furnish the regenerative tissue with a scaffold structure for neovasculature and a delivery system for an angiogenic growth factor. As such a scaffold structure, the present study created novel hydrogel materials by chemically cross-linking alkali-treated collagen (AlCol) with trisuccinimidyl citrate (TSC).

Materials and Methods: Many prototypes, consisting of several concentrations of TSC and AlCol, were implanted into the subfascial space of the rat rectus muscle, and 7 days later, the implanted materials were excised for histological analysis. Cross-sections were stained and neovascular development in the materials was evaluated by measuring vessel density, length and number of joints and branches.

Results: Significant ingrowth of vascularized granulation was observed in some materials, which surpassed the angiogenic ability of MatrigelTM. Further, combination with basic fibroblast growth factor (bFGF) significantly increased the vascular formation in these gels.

Conclusions: The TSC-AlCol gel functioned as a favorable scaffold for neovascular formation and also as a reservoir for controlled delivery of bFGF.

Key words: neovascular formation, hydrogel, collagen, citric acid, basic fibroblast growth factor

INTRODUCTION

Recent advances in the fields of tissue engineering and stem cell biology have produced practical regenerative tissues, some of which have been applied in clinical settings for therapeutic purposes.^{1,2)} However, at present, there are few regenerative products that completely

reproduce or simulate the function of the original tissue or organ. One crucial reason for the unfavorable status is insufficient development of technology to construct the three-dimensional (3-D) structure of regenerative tissues.³⁾ If these 3-D technologies could be applied for tissue engineering, it would be possible to produce highly-organized regenerative tissues with reasonable bulk, which would assure high performance of function and a long lifetime. In the construction of 3-D regenerative tissue, the most important step might be the formation of a vascular system in the tissue.⁴⁾ All tissues and organs require a supply of oxygen and nutrition and have to eliminate carbon dioxide and other metabolites. When the regenerative tissue is small enough, these processes can be accomplished by passive diffusion of environmental fluid, suggesting that blood perfusion is not always necessary in such a situation. In contrast, 3-D regenerative tissue with larger bulk requires blood perfusion through a

¹Division of Vascular Surgery, Department of Surgery, Graduate School of Medicine, The University of Tokyo, Tokyo, Japan

²Division of Tissue Engineering, The University of Tokyo Hospital, Tokyo, Japan

³Biomaterials Center, National Institute for Materials Science, Tsukuba, Ibaraki, Japan

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Corresponding author: Hiroyuki Koyama, MD. Division of Tissue Engineering, The University of Tokyo Hospital, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033, Japan

Tel: +81-3-5800-8653, Fax: +81-3-3811-6822

E-mail: hkoyama-ky@umin.ac.jp

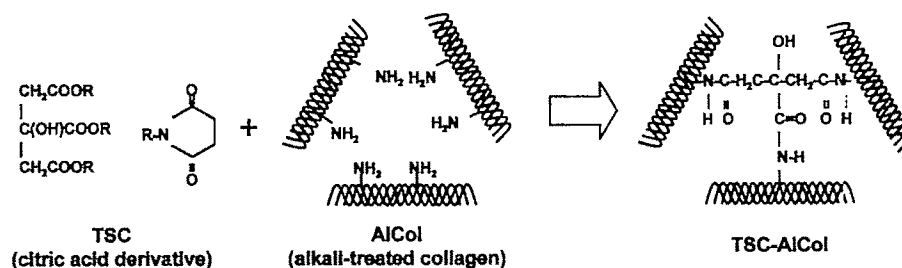


Fig. 1 Schematic illustration of chemically cross-linking reaction of citric acid derivative (TSC) with alkali-treated collagen (AICol).

vascular system to maintain the viability of the whole tissue, since the range of transportation by passive diffusion is limited to 100–200 μm at maximum.⁵⁾

Several approaches have been proposed to develop a vascular system in regenerative tissues, and one promising approach is induction of newly-formed vessels from the host vasculature by controlling vasculogenesis, angiogenesis or arteriogenesis.⁴⁾ Delivery of angiogenic growth factors or endothelial precursor cells potentially promotes these mechanisms of neovascularization, and this strategy has been applied for the treatment of vascular occlusive disease, such as ischemic heart disease and chronic limb ischemia.^{6–8)} However, to induce vessel formation in regenerative tissue, it is also important that the tissue is suitably furnished with a scaffold structure for newly-formed vessels, since it is essential for vessels *in vivo* to have a surrounding extracellular matrix (ECM) as a natural scaffold.⁹⁾ The vascular wall must be supported by ECM, and vascular cells receive several stimulants and signals via the matrix.⁹⁾ MatrigelTM, a preparation of basement membrane, is a well-known biomaterial that possibly serves as favorable scaffold for neovascularization, though it is difficult to utilize the material for clinical purposes, because it is extracted from mouse sarcoma.^{10, 11)}

As a safe biomaterial to induce neovascular ingrowth, we previously developed physical gel matrix which was an ion complex of atelocollagen and alkali-treated collagen (AICol) modified with trisuccinimidyl citrate (TSC).¹²⁾ In the present study, we created a chemical gel matrix for the same purpose. This hydrogel matrix was formed by chemically cross-linking AICol with TSC,^{13–15)} and can be combined with a potent angiogenic growth factor, basic fibroblast growth factor (bFGF). Application of this biomaterial in regenerative tissue is expected to lead to development of a vascular network in the regenerative tissue after implantation *in vivo*.

Table 1 Formulation of synthesized TSC-AICol gels

TSC (mM)	AICol (w/v %)				
	7.5	10	15	20	30
1	NA	NA	NA	NA	NA
3	NA	NA	+	+	+
6	+	+	+	+	+
10	+	–	–	–	–

NA: Gels were completely disappeared.

+: Granulation developed into gels

–: No granulation developed into gels

TSC, trisuccinimidyl citrate

MATERIALS AND METHODS

Synthesis of hydrogel matrix from TSC and AICol (TSC-AICol gel)

TSC was prepared as described previously.¹³⁾ Briefly, citric acid was dissolved in tetrahydrofuran (THF), and then hydroxysuccinimide (HOSu) and dicyclohexylcarbodiimide (DCC) were added. This mixture was concentrated with rotary evaporation under reduced pressure, and recrystallized to yield TSC. The obtained TSC was characterized by ¹H-NMR (JEOL EX-300) and elemental analysis: ¹H-NMR (DMSO-*d*₆) δ = 2.8 ppm (s, 12H, succinimidyl esters $\text{CH}_2 \times 6$), 3.4 ppm (s, 4H, $\text{CH}_2 \times 2$), 7.2 ppm (s, 1H, OH). Analysis: Calculated for $\text{C}_{18}\text{H}_{17}\text{N}_3\text{O}_3$: C, 44.73; H, 3.55; N, 8.69. Found: C, 44.83; H, 3.45; N, 8.58.

For the synthesis of TSC-AICol matrices, AICol (type I, derived from pig skin, Nitta Gelatin Inc., Osaka, Japan) was dissolved in dimethylsulfoxide (DMSO) to obtain 7.5, 10, 15, 20 and 30% w/v AICol solutions. Then, 50 μl TSC solution at a concentration of 1, 3, 6 or 10 mM was added to 200 μl of each AICol diluent. The TSC-AICol mixtures were poured into flat containers so as to be 1 mm thick and incubated for 24 h at 37°C to chemically cross-link AICol with TSC, forming gel sheets (Fig. 1).

The gel sheets were subsequently immersed in excess 0.1 M phosphate buffer solution for 24 h at 37°C to remove DMSO, and disc-shaped gels with 6 mm diameter were cut out from the gel sheets (1 mm thick) for in vivo implantation. In the present study, we synthesized twenty kinds of TSC-AICol gels for evaluation (**Table 1**) and abbreviated the TSC-AICol gel with formulation X mM TSC and Y % AICol to TSC[X]-AICol[Y].

Animal model and implantation of TSC-AICol matrices

Male Sprague-Dawley rats (3–4 months, Nisseizai, Tokyo, Japan) fed a normal diet were used in all experiments, and all protocols were conducted according to the Guide for Animal Experimentation of The University of Tokyo. Rats were anesthetized by intraperitoneal injection of sodium pentobarbital (50 mg/kg body wt). The rectus sheath was exposed through a middle incision of the abdomen, a longitudinal fasciotomy of the rectus sheath was carried out near the linea alba, and an appropriate space for implantation was prepared between the rectus sheath and the rectus abdominus muscle. After insertion of each TSC-AICol gel disc (n = 6 for each gel disc) in the subfascial space, the rectus sheath was closed with polypropylene sutures. In another set of animals, a flat drop (30 µl, ca. 37 µg) of Matrigel™ (BD Biosciences, CA, USA) was implanted in the same manner (n = 6). The volume of 30 µl Matrigel™ was almost the same as that of the TSC-AICol gel disc (6 mm diameter, 1 mm thick), and the flat drop of Matrigel™ was arranged in a similar shape to that of the TSC-AICol gel disc before gelation.

At 7 days after implantation, these implants were excised with the surrounding rectus sheath and muscle tissue, fixed with 4% phosphate buffered paraformaldehyde (0.1 mol/l PO₄ buffer, pH 7.3) overnight, and embedded in paraffin.

Analysis of neovascular development in the TSC-AICol gel

Each paraffin block was trimmed in order to expose the maximal transverse profile of the implanted materials, and 4-µm-thick cross-sections were cut. All sections were stained with hematoxylin & eosin. Then, other sets of cross-sections were stained for lectin to identify endothelial cells lining blood vessels.¹⁶⁾ The sections were first treated with 1% trypsin (Roche Applied Science) for 10 minutes, and then incubated with 3% hydrogen peroxide for 10 minutes. Subsequently, biotinylated lectin (L5391, Sigma, St. Louis, MO, USA) was applied at a 1:50

dilution for 2 hours at room temperature, and DAB treatment was carried out to develop brown color. Photomicrographs of cross-sections were taken with a digital microscope (BZ-9000, Keyence, Osaka, Japan) to analyze neovascular development in the implanted material. Since neovascularization in the material must progress from the tissue surrounding the material, analysis of cross sections was restricted to the peripheral region of each material, which was within 200 µm from the overall margin of the material profile, and the area of analysis was first measured with Image J software (National Institutes of Health, USA). Another reason for setting the analysis area within 200 µm from the margin was to eliminate the potential influence of a slight difference in implant shape and/or deformation. Then, using angiogenesis image analyzer software (KURABO, Kurabo, Osaka, Japan), the digital data of photomicrographs were binarized at a pre-set threshold, and the pixels that constituted blood vessels were counted in each binarized image.¹⁷⁾ The images were furthermore converted into line images by a thinning process, and the length of vessels and the number of vessel joints and branches were measured. Parameters for neovascular development were calculated as follows.

Vessel density (pixels/µm²) = pixels of blood vessels / analysis area

Vessel length (µm/µm²) = length of vessels / analysis area

Vessel joints (/µm²) = number of vessel joints / analysis area

Vessel path (/µm²) = number of vessel branches / analysis area

Analysis of the images was repeated twice in a blinded manner by a student helper, and the mean of the three values was used for statistical analysis.

Combination of bFGF with TSC-AICol gel

To evaluate what amount of bFGF potentially combines with the TSC-AICol gel, the gels were incubated with sufficient bFGF, and the amount of combined bFGF was measured. An excess (1 µg) of human recombinant bFGF (R&D Systems, MN, USA) was added to three kinds of TSC-AICol gel discs (6 mm diameter and 1 mm thick, n = 4 each) whose formulation was 3, 6 or 10mM TSC and 15% AICol (TSC[3, 6, 10]-AICol 15). After 3 hours of incubation in a humid chamber at room temperature, the gel discs were washed three times with PBS to remove uncombined bFGF. Then, the bFGF-treated gel disc was homogenized and lysed in 100 µl high-salt

buffer (50mM Tris [pH7.6], 1.5M NaCl, 1 mM PMSF, 10 µg/ml leupeptin), and the volume of the lysate was measured (V_{LYSATE}). The concentration of bFGF in the lysate (C_{bFGF}) was quantified by ELISA using a bFGF ELISA kit (R&D Systems) according to the manufacturer's instructions, and the amount of bFGF bound to each gel disc was calculated as $V_{\text{LYSATE}} \times C_{\text{bFGF}}$.

Vascular development after implantation of bFGF-treated TSC-AICol gels

Another series of TSC-AICol gel discs (Fig. 1B) was incubated with 1 µg bFGF for 3 hours at room temperature, and washed three times with PBS. The bFGF-treated gel discs were implanted into the subfascial space of the rat abdomen. At 7 days after implantation, the implants were resected from the animals, and vascular development in the gels was evaluated in the same manner.

Statistical analysis

All data are presented as mean $\pm$ SE for each group. Student's *t*-test was used for comparison of each group. *P* values < 0.05 were considered statistically significant.

RESULTS

Synthesis of TSC-AICol gels

The gels were successfully synthesized in the presented formulations (Table 1). Reaction solvent, DMSO, was completely substituted by water. The color of the gels was water-clear, and the shape and hardness of the gels were stable in water for more than 1 month. As the concentration of TSC or AICol decreased, the hardness of the synthesized gels became softer. In addition to the presented formulations, we tried to make TSC-AICol mixtures whose concentration of AICol was 5% or less; however, these mixtures did not gelate, irrespective of AICol concentration.

Histological findings of excised implants

Histological analysis with hematoxylin & eosin staining showed the in vivo status of each material at 7 days after implantation, and also revealed how granulation development and inflammatory reactions were induced in and around the material on the same day. After implantation of TSC [1]-AICol [7.5, 10, 15, 20, 30] and TSC [3]-AICol [7.5, 10] gels, the structure of the gels completely disappeared, and no accumulation of inflammatory cells was detected around the implanted site. In

contrast, other TSC-AICol gels and Matrigel™ maintained their gel structure even at 7 days after implantation. Regarding granulation growth into the residual material, a certain amount of granulation tissue developed with inflammatory infiltration in TSC [3]-AICol [15, 20, 30], TSC [6]-AICol [7.5, 10, 15, 20, 30], TSC [10]-AICol [7.5], and Matrigel™, whereas little growth of granulation tissue was observed in TSC [10]-AICol [10, 15, 20, 30] (Fig. 2).

Neovascular development after implantation of the TSC-AICol gel

Histological staining for lectin successfully demonstrated the distribution of the vasculature in host tissue and also in the implanted materials. Vascular development into the implanted materials was detected in TSC [3]-AICol [15, 20, 30], TSC [6]-AICol [7.5, 10, 15, 20, 30], TSC [10]-AICol [7.5], and Matrigel™ (Fig. 2). All parameters of neovascular development showed that values in TSC [3]-AICol [15], TSC [6]-AICol [7.5, 10, 15] and TSC [10]-AICol [7.5] were significantly higher than those in Matrigel™ (Fig. 3).

Combination of bFGF with the TSC-AICol gel

Three kinds of TSC-AICol gels (TSC [3, 6, 10]-AICol [15]) were treated with a sufficient volume of bFGF, and ELISA analysis for bFGF showed that bFGF constantly bound to each TSC-AICol gel. The amount of bFGF bound to TSC [3]-AICol [15] was significantly greater than that bound to TSC [6]-AICol [15] and TSC [10]-AICol [15], while there was no difference between the values of TSC [6]-AICol [15] and TSC [10]-AICol [15] (Fig. 4).

Vascular development after implantation of bFGF-treated TSC-AICol gels

The combination of bFGF significantly increased vessel density and length in TSC [3]-AICol [15], TSC [6]-AICol [7.5, 10] and TSC [10]-AICol [7.5], as compared with those in untreated gels (Fig. 3A and 3B). Further, the vessel joints and path showed significantly higher values in bFGF-treated gels than in untreated plain gels (Fig. 3C and 3D).

DISCUSSION

A scaffold structure is essential for induction of neovascular growth into regenerative tissues, since neovascularity requires surrounding supportive tissues to maintain

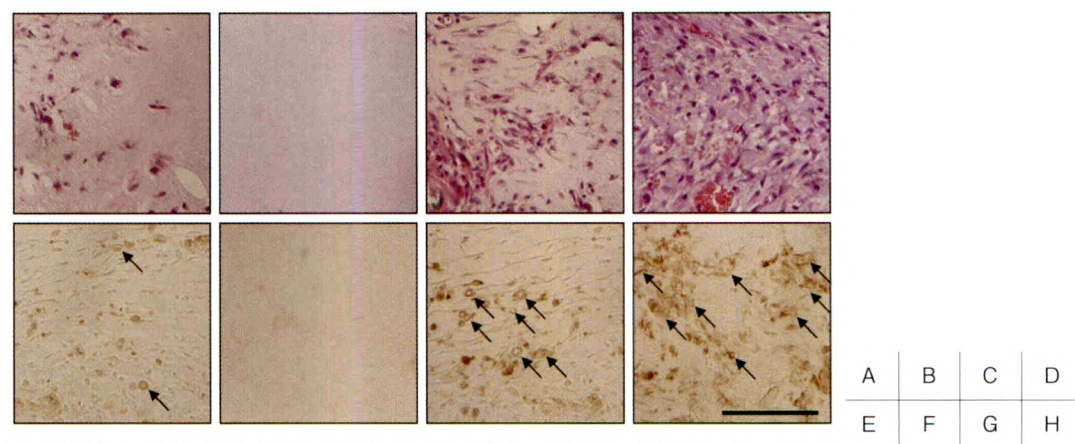


Fig. 2 Photomicrographs of excised implants at 7 days after implantation into the rat subfascial space. Presented micrographs are from implants of Matrigel (A, E), TSC [10]-AICol [10] (B, F), TSC [6]-AICol [10] (C, G) and bFGF-combined TSC [6]-AICol [10] (D, H). Sections were stained with hematoxylin & eosin (A, B, C, D), and also stained for lectin to detect vessels (E, F, G, H). There was no tissue growth into TSC [10]-AICol [10] implants (B, F), whereas granulation and vessel growth (arrow) were noted in other implants. Bar: 50 μ m

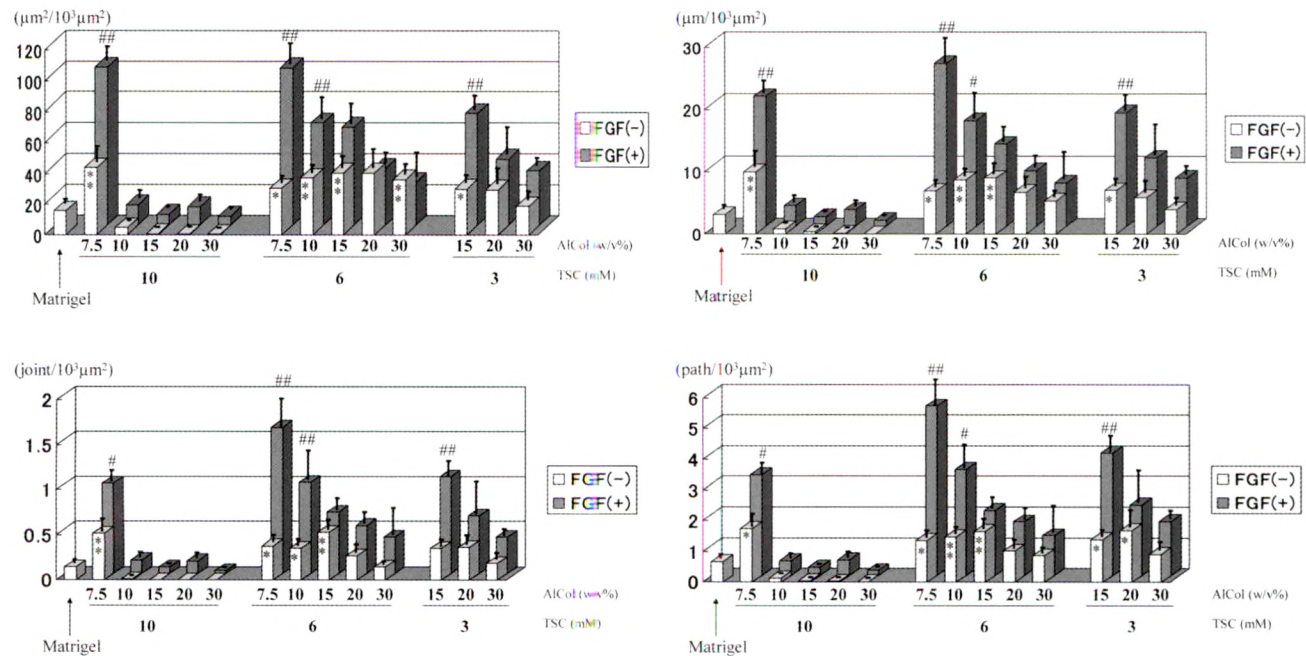


Fig. 3 Quantitative analysis of lectin staining. Vessel density, vessel length, vessel joints and vessel path in the part analyzed were measured. Values are shown as mean $\pm$ SD (n = 6). *P < 0.05 vs Matrigel, **P < 0.01 vs Matrigel, #P < 0.05 non-treated gel vs bFGF-combined gel, ##P < 0.01 non-treated gel vs bFGF-combined gel.

its luminal structure and biological performance.⁹⁾ In the present study, we developed a novel gel material that could function as a scaffold for neovascular growth. Many prototypes of hydrogel material were made by incorporating several concentrations of TSC and AICol, and implanted into the subfascial space of the rat rectus

muscle. Although some prototypes induced no growth of vasculature, gels with appropriate concentrations of TSC and AICol markedly promoted neovascular formation in the gels at 7 days after implantation, which surpassed the angiogenic ability of MatrigelTM.

There are some possible reasons why TSC-AICol gels

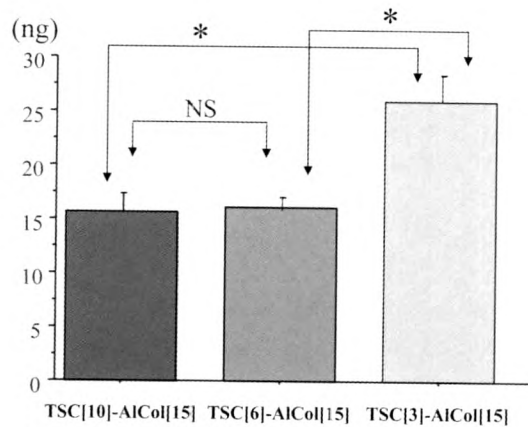


Fig. 4 Capacity of bFGF combination with TSC [10]-AICol [15], TSC [6]-AICol [15] and TSC [3]-AICol [15] gel discs (6 mm diameter, 1 mm thick). An excess amount of bFGF was added to each gel, and 3 hours later, combined bFGF was measured. Values are shown as mean $\pm$ SD ($n = 4$). * $P < 0.05$, NS: not significant.

induced favorable growth of vascularized tissue into the material. One crucial reason might be that the TSC-AICol gel provided a suitable matrix microstructure as a platform for vessel formation. In vivo, vessels are naturally included in ECM, and ECM possesses the character of a hydrogel. Thus, it is not surprising that artificial hydrogel also reproduces a microstructure that mimics natural ECM.¹⁸⁾ Indeed, Zisch et al. synthesized an artificial hydrogel material based on polyethylene glycol (PEG) and synthetic peptides, and showed that vascularized tissue grew into the hydrogel material after implantation into the rat subcutis.¹⁹⁾ To realize such ECM-mimicking properties, however, the polymer network of the artificial hydrogel must have an adequate density. If the network of the polymer structure is too dense, vascular growth into the hydrogel could be physically blocked, and if the interstitial distance of the network is too large, the microstructure of the hydrogel would not sustain the surrounding wall of the neovasculature as a scaffold. In the present study, no growth of vasculature was observed in some prototypes, possibly indicating that their microstructure did not provide appropriate space for neovascular formation. Further, the combination of bFGF significantly promoted neovascular formation in some prototypes, in which vascular development was seemingly observed more in the hydrogel containing less AICol. It possibly indicates that too dense TSC and AICol would interfere with vascularization especially in the bFGF treated hydrogels because once bFGF was impregnated larger quantity of vascular development occurred and

newly formed vessels themselves occupy certain extents of the space.

It is also important that the structure of the hydrogel contains cell adhesive sites to function as a scaffold for vascularized tissue. In vivo, ECM supports the vascular wall by anchoring vascular wall cells to matrix molecules. Attachment between vascular cells and surrounding ECM molecules is critical to establish the luminal structure of vessels and regulation of vessel growth.⁹⁾ In the mechanism of cell-ECM attachment, integrins play an important role as cell surface receptors.¹⁸⁾ Integrins are obligate heterodimers consisting of α and β subunits. In mammals, 19 α and 8 β subunits have been characterized, and more than 20 types of integrins with different combinations of α and β subunits have been identified.²⁰⁾ Each integrin respectively binds with unique ECM components. As a matter of course, endothelial and other vascular cells also express several kinds of integrins on their cell membrane,²¹⁾ and some of these integrins can directly bind with collagen.²²⁾ However, the predominant integrin-ligand in cell-ECM attachment is fibronectin, a high-molecular-weight glycoprotein.²³⁾ Especially, fibronectin is known to be a potent ligand of $\alpha_4\beta_3$ and $\alpha_5\beta_1$, which are critical integrins in neovascularization and granulation formation.²¹⁾ Fibronectin is abundantly contained in blood plasma in its soluble form, and it is also able to potently associate with collagen molecules.²³⁾ Therefore, in the in vivo condition, which is fibronectin-rich, integrins on the cell surface possibly bind with collagen molecules through the intermediary of sufficient fibronectin. These properties of collagen molecules suggest that TSC-AICol gels possess adequate cell adhesive sites in their structure to function as a scaffold.

Another possible reason explaining the vascularization ability of the TSC-AICol gel might be that the appropriate part of the gel was degraded according to neovascular growth into its inside. In this regard, it is critical that gel degradation should occur only in the direction of neovascular growth, and the other part of the gel structure must be preserved as a scaffold for newly formed vessels. For elongation and enlargement of vessels in vivo, vascular wall cells and infiltrating cells in ECM generally release a variety of proteases, such as matrix metalloproteinases (MMPs) and plasminogen activators (PAs), and promote the degradation of a surrounding ECM to ensure space for vessel growth.^{24, 25)} Therefore, the scaffold material for ingrowth of vascularized tissue must contain protease-cleavable sites and concomitantly possess stability against variable local

situations except angiogenic proteases. Collagen molecules contain abundant MMPs-cleavable sites,²⁶⁾ indicating that collagen is a potential material for induction of neovascularization. Indeed, a previous *in vitro* study showed that tube formation of endothelial cells was accelerated under culture in a gelled emulsion of collagen.²⁷⁾ This evidence demonstrated that gelled collagen was successfully remodeled *in vitro* according to neovascularization, and also functioned as a scaffold for newly formed vessels. However, since collagen molecules are merely entangled in the emulsion form, a gelled emulsion of collagen might be dissolved by adding excessive fluid. If such a collagen material is implanted under physiological conditions *in vivo*, exudates accumulated around the implant consequentially dilute the collagen and then cause disintegration of its structure as a scaffold. Therefore, it is necessary to cross-link collagen molecules to stabilize the gel structure. Since the TSC-AICol gel is a chemical gel in which collagen molecules are cross-linked by a citric acid derivative, TSC-AICol gel enabled maintenance of a scaffold structure for vascular tissue, while only the gel part in the direction of vessel growth was digested by released proteases.

Further, the citric acid-based crosslinker, TSC also functions as a reservoir of bFGF. In general, angiogenic humoral factors play important roles in the induction of neovascularization, and previous studies have demonstrated several growth factors and cytokines to be angiogenic factors.⁵⁾ Each angiogenic factor possesses specific functions that contribute to neovascularization, and appropriate combinations of these functions promote appropriate vessel formation according to situational demand. Indeed, there are three processes in the formation of new vessels; vasculogenesis, angiogenesis and arteriogenesis, and these processes are generally induced by distinctive combinations of angiogenic factors.²⁸⁾ Vasculogenesis in the adult represents a process by which endothelial progenitor cells differentiate and replicate to form a primitive network of vasculature, and angiogenesis is the process of endothelial migration and replication resulting in the formation of a capillary network. In contrast, arteriogenesis refers to the maturation and enlargement processes of preexisting small vessels, which increases the conducting ability of the blood vessels. The proposed function of the TSC-AICol gel is to promote neovascular ingrowth from the surrounding host vasculature, followed by construction of a mature network of blood perfusion in the area of existing gel. It is, therefore, desirable that the TSC-AICol gel enables induction of the

process of arteriogenesis in addition to angiogenesis and/or vasculogenesis. Since bFGF is known to induce angiogenesis and arteriogenesis,^{6, 28)} it is an ideal angiogenic factor for increasing the effect of vascular development in the TSC-AICol gel. Further, it might be important that bFGF associated with the TSC-AICol gel. When bFGF solution is added to the TSC-AICol gel, bFGF molecules might permeate through the matrix structure of the TSC-AICol gel and then bind to the TSC part with ionic bonds, because bFGF is positively charged and TSC is negatively charged.¹³⁾ Therefore, there is a reserve of bFGF inside the TSC-AICol gel, which stimulates the vessels that have grown into the gel, accelerating vascular development inside the gel. The present study indeed revealed that combination with bFGF significantly increased vascular formation in the TSC-AICol gel. Further, measurement of bFGF level also showed that the concentration of combined bFGF in the TSC-AICol gel was reasonable for proliferation of ordinary cells, though it might be necessary to clarify the relation between TSC concentration and combined bFGF level.²⁹⁾ If the TSC-AICol gel is unable to bind with bFGF, bFGF in the gel might spread to the outside after implantation, and neovascularization might be induced only around the gel.

In summary, we created novel hydrogel materials by incorporating several concentrations of TSC and AICol, and an *in vivo* study using a rat model showed that some of these materials had induced marked growth of vasculature-rich tissue into the inside of the materials at 7 days after implantation. Further, the ability of vascular ingrowth was significantly enhanced by combining bFGF with the materials. These findings suggest that the hydrogel materials functioned as a favorable scaffold for neovascular formation and also as a reservoir for controlled delivery of bFGF.

REFERENCES

- 1) MacNeil S. Progress and opportunities for tissue-engineered skin. *Nature* 2007; **445**: 874-80.
- 2) Raghunath J, Rollo J, Sales KM, Butler PE, Seifalian AM. Biomaterials and scaffold design: key to tissue-engineering cartilage. *Biotechnol Appl Biochem* 2007; **46**: 73-84.
- 3) Levenberg S, Rouwkema J, Macdonald M, Garfein ES, Kohane DS, Darland DC, et al. Engineering vascularized skeletal muscle tissue. *Nat Biotechnol* 2005; **23**: 879-84.
- 4) Rouwkema J, Rivron NC, van Blitterswijk CA. Vascularization in tissue engineering. *Trends Biotechnol* 2008; **26**: 434-41.

- 5) Carmeliet P, Jain RK. Angiogenesis in cancer and other diseases. *Nature* 2000; **407**: 249-57.
- 6) Hosaka A, Koyama H, Kushibiki T, Tabata Y, Nishiyama N, Miyata T, et al. Gelatin hydrogel microspheres enable pinpoint delivery of basic fibroblast growth factor for the development of functional collateral vessels. *Circulation* 2004; **110**: 3322-8.
- 7) Ninomiya M, Koyama H, Miyata T, Hamada H, Miyatake S, Shigematsu H, et al. Ex vivo gene transfer of basic fibroblast growth factor improves cardiac function and blood flow in a swine chronic myocardial ischemia model. *Gene Ther* 2003; **10**: 1152-60.
- 8) Tateishi-Yuyama E, Matsubara H, Murohara T, Ikeda U, Shintani S, Masaki H, et al. Therapeutic angiogenesis for patients with limb ischaemia by autologous transplantation of bone-marrow cells: a pilot study and a randomised controlled trial. *Lancet* 2002; **360**: 427-35.
- 9) Davis GE, Senger DR. Endothelial extracellular matrix: biosynthesis, remodeling, and functions during vascular morphogenesis and neovessel stabilization. *Circ Res* 2005; **97**: 1093-107.
- 10) Kleinman HK, McGarvey ML, Liotta LA, Robey PG, Tryggvason K, Martin GR. Isolation and characterization of type IV procollagen, laminin, and heparan sulfate proteoglycan from the EHS sarcoma. *Biochemistry* 1982; **21**: 6188-93.
- 11) Passaniti A, Taylor RM, Pili R, Guo Y, Long PV, Haney JA, et al. A simple, quantitative method for assessing angiogenesis and antiangiogenic agents using reconstituted basement membrane, heparin, and fibroblast growth factor. *Lab Invest* 1992; **67**: 519-28.
- 12) Takayama T, Taguchi T, Koyama H, Sakari M, Kamimura W, Takato T, et al. The growth of a vascular network inside a collagen-citric acid derivative hydrogel in rats. *Biomaterials* 2009; **30**: 3580-7.
- 13) Saito H, Taguchi T, Aoki H, Murabayashi S, Mitamura Y, Tanaka J, et al. pH-responsive swelling behavior of collagen gels prepared by novel crosslinkers based on naturally derived di- or tricarboxylic acids. *Acta Biomater* 2007; **3**: 89-94.
- 14) Saito H, Murabayashi S, Mitamura Y, Taguchi T. Unusual cell adhesion and antithrombogenic behavior of citric acid-cross-linked collagen matrices. *Biomacromolecules* 2007; **8**: 1992-8.
- 15) Taguchi T, Saito H, Iwasashi M, Sakane M, Kakinoki S, Ochiai N, et al. Development of a novel glue consisting of naturally-derived biomolecules: citric acid and human serum albumin. *J Nanosci Nanotechnol* 2007; **7**: 742-7.
- 16) Fujihara Y, Koyama H, Ohba M, Tabata Y, Fujihara H, Yonehara Y, et al. Controlled delivery of bFGF to recipient bed enhances the vascularization and viability of an ischemic skin flap. *Wound Repair Regen* 2008; **16**: 125-31.
- 17) Oike Y, Ito Y, Maekawa H, Morisada T, Kubota Y, Akao M, et al. Angiopoietin-related growth factor (AGF) promotes angiogenesis. *Blood* 2004; **103**: 3760-5.
- 18) Lutolf MP, Hubbell JA. Synthetic biomaterials as instructive extracellular microenvironments for morphogenesis in tissue engineering. *Nat Biotechnol* 2005; **23**: 47-55.
- 19) Zisch AH, Lutolf MP, Ehrbar M, Raeber GP, Rizzi SC, Davies N, et al. Cell-demanded release of VEGF from synthetic, biointeractive cell ingrowth matrices for vascularized tissue growth. *FASEB J* 2003; **17**: 2260-2.
- 20) Hynes RO. Integrins: bidirectional, allosteric signaling machines. *Cell* 2002; **110**: 673-87.
- 21) Ruegg C, Dormond O, Mariotti A. Endothelial cell integrins and COX-2: mediators and therapeutic targets of tumor angiogenesis. *Biochim Biophys Acta* 2004; **1654**: 51-67.
- 22) Tulla M, Pentikainen OT, Viitasalo T, Kapyla J, Impola U, Nykvist P, et al. Selective binding of collagen subtypes by integrin alpha 1I, alpha 2I, and alpha 10I domains. *J Biol Chem* 2001; **276**: 48206-12.
- 23) Pankov R, Yamada KM. Fibronectin at a glance. *J Cell Sci* 2002; **115**: 3861-3.
- 24) Ghajar CM, Blevins KS, Hughes CC, George SC, Putnam AJ. Mesenchymal stem cells enhance angiogenesis in mechanically viable prevascularized tissues via early matrix metalloproteinase upregulation. *Tissue Eng* 2006; **12**: 2875-88.
- 25) Brodsky S, Chen J, Lee A, Akassoglou K, Norman J, Goligorsky MS. Plasmin-dependent and -independent effects of plasminogen activators and inhibitor-1 on ex vivo angiogenesis. *Am J Physiol Heart Circ Physiol* 2001; **281**: H1784-92.
- 26) Woessner JF Jr. Matrix metalloproteinases and their inhibitors in connective tissue remodeling. *FASEB J* 1991; **5**: 2145-54.
- 27) Madri JA, Pratt BM. Endothelial cell-matrix interactions: in vitro models of angiogenesis. *J Histochem Cytochem* 1986; **34**: 85-91.
- 28) van Royen N, Piek JJ, Buschmann I, Hoefer I, Voskuil M, Schaper W. Stimulation of arteriogenesis; a new concept for the treatment of arterial occlusive disease. *Cardiovasc Res* 2001; **49**: 543-53.
- 29) Labitzke R, Friedl P. A serum-free formulation supporting growth of human umbilical cord vein endothelial cells in long-term cultivation. *Cytotechnology* 2001; **35**: 87-92.

» **Original Article** «

Preoperative Non-ambulatory Status Predicts Poor Outcome after Below Knee Bypass Surgery

Kota Yamamoto, MD, PhD, Tadashi Kitaoka, MD, Harunobu Matsumoto, MD, Juno Deguchi, MD, PhD, and Osamu Sato, MD, PhD

Objective: To identify the outcome of below knee bypass that focuses on the functional status and to investigate whether preoperative functional status can predict these outcomes.

Materials and Methods: One hundred and fifty one limbs in one hundred and thirty two patients that underwent below knee bypass between 2004 and 2008 were retrospectively reviewed. The patients were grouped as “ambulatory,” “non-ambulatory transfer” and “non-ambulatory bedridden,” according to their functional status. Clinical success was defined as the achievement of all of following end points; graft patency to wound healing, limb salvage for 1 year or until death, maintenance of ambulatory status for 1 year, and survival for 6 months. The effect of preoperative ambulatory status was analyzed.

Results: The overall primary and secondary graft patency, limb salvage and survival at 1 year were 76.3%, 81.8%, 89.1% and 84.1%, respectively. The overall success rate was 62.0%. Clinical success rates for the ambulatory and non-ambulatory groups were 75.6% and 34.9% ($P = 0.0009$, OR: 4.4; 95% CI: 1.8–10.6).

Conclusions: Bypass surgery is justified for maintaining the independent status of ambulatory patients. On the other hand, the high likelihood of poor outcomes for non-ambulatory patients must be considered before performing bypass surgery.

Key words: below knee bypass, ambulatory status, clinical success rate, risk factors

INTRODUCTION

Due to an upward trend in the prevalence of risk factors for atherosclerosis, especially diabetes,¹⁾ the prevalence of peripheral arterial disease (PAD) is estimated to be increasing in Japan over the last decade. This has led to an increase in the number of patients undergoing bypass surgery and radiological intervention. Despite these therapies, the main outcomes, such as patency and limb salvage, remain as described by Rutherford in 1997.²⁾

Cardiovascular disease in patients with critical limb ischemia imposes obvious limitations on life expectancy. Thus, preserving functional status and minimizing complications after intervention for peripheral arterial occlusive disease are equally important to limb salvage and graft patency.

In this study, we examined the results of below-knee bypass based on various factors including ambulatory status and survival. And because we have focused on ambulatory status as one of the main outcome, this study also investigated whether preoperative ambulatory status affects the outcome of bypass surgery.

MATERIALS AND METHODS

This study proceeded following the guidelines of the research ethics committee of our institution between January 2004 and December 2008. We obtained written, informed consent from patients with limb ischemia to

Department of Vascular Surgery, Saitama Medical Center, Saitama Medical University, Kawagoe, Saitama, Japan

Received: January 4, 2011; Accepted: April 7, 2011
Corresponding author: Kota Yamamoto, MD, PhD. Department of Vascular Surgery, Saitama Medical Center, Saitama Medical University, 1981 Kamoda, Kawagoe, Saitama 350-0844, Japan
Tel: +81-49-228-3462, Fax: +81-49-228-3462
E-mail: k-yamamo@tc4.so-net.ne.jp

perform below-knee bypasses. As a basic rule, we performed bypass surgery on all patients visiting our hospital with ischemic symptoms due to peripheral arterial disease. If bypass surgeries were possible to perform, we would offer bypass surgeries regardless of the patients' mental status. We did not perform bypass surgery on patients who were regarded to be unable to tolerate the operation due to their medical comorbidities, had no recipient artery to perform a bypass, had infection or gangrene invading the site of anastomosis, had no vein usable as a graft, or refused to undergo the operation. Due to our policy, we did not perform any endovascular interventions on infrainguinal lesions.

The recorded preoperative characteristics were age, sex, hypertension, diabetes, renal failure, smoking status, serum albumin values, ejection fraction measured by transthoracic echocardiography as means of heart failure, sites of distal anastomosis and ambulatory status at 1 month before the onset of their ischemic symptoms. Patients were regarded as ambulatory if they could walk with or without a cane. As reported by Taylor, non-ambulatory patients were further classified as "non-ambulatory-transfer" if they could move into a wheelchair unassisted and the remaining patients were regarded as "non-ambulatory-bedridden."³⁾ For patients undergoing surgeries for bilateral limbs, data regarding the first surgery was used. When the surgery was performed simultaneously for both limbs, the more critical limb was analyzed.

A vein graft (reversed, non-reversed transposed or in situ) was applied in all surgeries under total limb ischemia accomplished with a pneumatic tourniquet (non-dissection method).⁴⁻⁶⁾ Postoperative computed tomography (CT) or angiography was performed 1-2 weeks after surgery, and a second operation was performed when necessary. The patients were asked to attend the hospital at 1- to 2-month intervals after discharge so that the status of the operated limb could be recorded. The patency of the graft was assessed by pulsation and Duplex sonography.

The results of the bypass surgery were analyzed using traditional graft patency, limb salvage, survival rate and the factors introduced by Taylor.³⁾ A successful outcome was defined as the achievement of all of the following end points; graft patency to wound healing, limb salvage for 1 year or until death, maintenance of ambulatory status for 1 year and survival for 6 months. Transmetatarsal and toe amputations were regarded as limb salvage. Therefore, patients that were nonambulatory transfer preoperatively but nonambulatory bedridden postopera-

tively were regarded as a failure. Limb salvage was defined as the absence of lower limb shortening.

All data were analyzed using JMP 5.0 software (SAS Institute Inc.), and a P value of < 0.05 was considered significant in each analysis.

RESULTS

Between January 2004 and December 2008, two hundred and two patients visited our hospital for critical limb ischemia. Below knee bypass was performed on 151 limbs in 132 patients, primary amputation was performed in 13 patients, and 57 patients were regarded as non-operable. As a result, the bypass surgery was performed in 65.3% of patients. Nineteen patients required bypass surgery for the contralateral limb simultaneously or later.

Of 132 patients, 85 (64.4%) were ambulatory, and 47 (35.6%) were non-ambulatory. **Table 1** shows the baseline characteristics of the 132 patients. As in Table 1, all patients were operated for symptoms of critical limb ischemia, but 20 of the 85 ambulatory patients were severe claudicants one month before the operation. These claudicants had at least rest pain by the time of operation, which may seem a rapid change in ischemic condition. This was probably possible because we were able to perform most of the operation, especially patients whose symptoms changed rapidly, within one to two weeks after the first visit. The median follow up period was 14.5 months. The overall rates of primary and secondary graft patency, limb salvage and survival at 1 year were 76.8%, 81.1%, 89.2% and 83.8%, respectively. The overall clinical success rate was 62.3%.

First, we performed univariate risk analysis on 132 patients regarding clinical success rate. As shown in **Table 2**, statistically significant factors were; age > 80, non-ambulatory status and gangrenous symptoms. Although not significant, smoking status tended to have some effect on clinical success rate. We then underwent multivariate analysis limited to these four factors. As in **Table 3**, the only significant factor was non-ambulatory status ($P = 0.0005$, OR: 5.6; 95% CI: 2.2-15.3).

DISCUSSION

Due to the increasing prevalence of risk factors for cardiovascular disease,¹⁾ it can be deduced that the prevalence of PAD is increasing in Japan, as in other countries. Infrainguinal bypass has been established as a treatment for PAD over the past few decades, and although the

Table 1 Baseline characteristics of 132 patients

Age (mean $\pm$ SD)	68.5 $\pm$ 12.1
Sex (Male : Female)	102 : 30
Diabetes	86 (65.2%)
Hypertension	45 (34.1%)
End stage renal disease	45 (34.1%)
Smoking	66 (50.0%)
Albumin (mean $\pm$ SD)	3.5 $\pm$ 0.6
Indication for operation	
Rest pain	47 (35.7%)
Ulcer	20 (15.2%)
Gangrene $\pm$ infection	65 (49.2%)
Ambulatory status	
Ambulatory	85 (64.4%)
Non-ambulatory	47 (35.6%)
Low cardiac function (Ejection fraction < 50%)	19 (24.6%) (n = 77)
Distal anastomosis	
Below knee popliteal	30 (22.7%)
Posterior tibial	41 (31.1%)
Anterior tibial	15 (11.4%)
Tibioperoneal trunk	7 (5.3%)
Peroneal	17 (12.9%)
Dorsalis pedis	16 (12.1%)

Table 2 Univariate analysis for clinical success rate (n = 132)

Risk Factors	Clinical success rate		P value
	Factor present	Factor absent	
Age > 80	37.5%	66.3%	0.03
Male	66.3%	50.0%	0.12
Diabetes	60.0%	66.7%	0.48
Hypertension	52.6%	67.1%	0.14
End stage renal disease	55.0%	66.2%	0.24
Smoking	70.7%	53.6%	0.06
Albumin < 2.5	33.3%	63.9%	0.14
Non-ambulatory	32.4%	76.6%	< 0.0001
Gangrene $\pm$ infection	51.7%	73.2%	0.02
Low cardiac function	38.5%	45.7%	0.65
Distal anastomosis			0.14
	Below knee popliteal	80.8%	
	Posterior tibial	51.4%	
	Anterior tibial	53.8%	
	Tibioperoneal trunk	83.3%	
	Peroneal	53.3%	
	Dorsalis pedis	53.9%	
	Plantar	83.3%	

Table 3 Multivariate risk factor analysis for clinical success rate

	Odds ratio (95% CI)	P value
Age > 80	2.2 (0.6–7.9)	0.23
Smoking	1.7 (0.7–4.2)	0.23
Non-ambulatory	5.6 (2.2–15.3)	0.0005
Gangrene	1.3 (0.5–3.3)	0.61

status of endovascular treatment has increased, bypass surgery remains the treatment of first choice for lesions below the knee.

The outcomes of lower extremity bypass surgery are traditionally assessed as graft patency, limb salvage and patient survival. Many factors including anatomical disease extent, clinical presentation, and resource availability can influence these outcomes.⁷⁾ Despite the repeatedly documented ability of bypass surgery to achieve graft patency and limb salvage, legitimate concerns persist regarding the appropriate roles of these procedures.

One of the main concerns about bypass surgery is limited life expectancy, especially for patients with critical limb ischemia.⁸⁾ Given the evident limitations on life expectancy imposed by critical limb ischemia,⁷⁾ preserving functional status and minimizing complications after intervention for PAD are of equal importance to limb salvage and graft patency. Therefore, in addition to the traditional factors recommended by Rutherford,²⁾ we used Taylor's clinical success rate that included ambulatory status as a functional factor.³⁾ Using these tools, we showed that the outcome after 1 year is worse in functionally dependent patients. The clinical success rate was considerably poorer in the non-ambulatory than ambulatory patients (32.4% vs. 76.6%). We are convinced that this is not due to technical problems because our overall success rate of 62.2% was comparable with that reported by Taylor (44.4%).³⁾

We were quite surprised that end-stage renal disease (ESRD) did not turn out to be a risk factor in our study. Due to the limited number of patients especially those with ESRD, this study can only say that the preoperative ambulatory status is more powerful risk factor compared with ESRD.

These findings indicate that ambulatory status is not only an outcome measure in bypass surgery, but also a preoperative risk factor that closely correlates with success rates. Crawford has also shown that preoperative functional status can predict perioperative outcomes (30-day morbidity and mortality) after infrainguinal bypass.⁹⁾

Abou-Zamzam has reported that 99% of survivors who lived independently before surgery continued to do so after surgery, whereas only 4% of survivors who did not live independently before the surgery achieved independence thereafter.¹⁰⁾ Their study also concluded that preoperative non-ambulatory status and renal insufficiency or failure were independent predictors of death within 6 months. This report, together with our findings of better life expectancy for ambulatory patients (88.0%

at 1 year) justifies performing bypass surgery on ambulatory patients to maintain their independence and ambulatory status.

On the other hand, these results also indicate a need for awareness of the poor outcomes of bypass surgery for non-ambulatory patients; however, this does not mean that primary amputation should be the first consideration for such patients. The potential effects of these strategies should be carefully compared before reaching a conclusion.

For example, the length of hospital stay and cost effectiveness should be considered. Chung found that wounds had not healed after 1 year in 25% of patients who had undergone infrainguinal bypass to treat critical limb ischemia.¹¹⁾ These patients might remain in hospital longer and thus miss the opportunity to be fitted with an appropriate prosthesis.

Primary amputation is by no means a safe remedy. Although not a randomized control trial, Sottiurai found that 30-day mortality rates of patients after femorodistal revascularization, below-knee amputations and above-knee (primary) amputations were 2.1%, 6.3% and 13.3%, respectively.¹²⁾

Lastly, primary amputation does not improve the outcomes of non-ambulatory patients. Taylor identified non-ambulatory status as a preoperative risk factor for an unsuccessful outcome after major lower limb amputation.¹³⁾

CONCLUSION

Due to relatively high success and survival rates, bypass surgery is justified for maintaining the independent status of ambulatory patients. On the other hand, for the non-ambulatory patients, in addition to the low probability of regaining ambulatory status, the high likelihood of poor general outcomes must be considered. Further studies should compare bypass surgery and primary amputation to determine a better strategy for treating PAD.

REFERENCE

- 1) Kadota A, Miura K, Ueshima H. [Diabetes and cardiovascular disease in NIPPON DATA]. *Nippon Rinsho* 2010; **68**: 847-52. (in Japanese)
- 2) Rutherford RB, Baker JD, Ernst C, Johnston KW, Porter JM, Ahn S, et al. Recommended standards for reports dealing with lower extremity ischemia: revised version. *J Vasc Surg* 1997; **26**: 517-38.

- 3) Taylor SM, Cull DL, Kalbaugh CA, Cass AL, Harmon SA, Langan EM 3rd, et al. Critical analysis of clinical success after surgical bypass for lower-extremity ischemic tissue loss using a standardized definition combining multiple parameters: a new paradigm of outcomes assessment. *J Am Coll Surg* 2007; **204**: 831-8.
- 4) Bernhard VM, Boren CH, Towne JB. Pneumatic tourniquet as a substitute for vascular clamps in distal bypass surgery. *Surgery* 1980; **87**: 709-13.
- 5) Sato O, Miyata T, Shindo S, Takayama Y, Tada Y. Nondissection method in distal arterial bypass surgery. *Acta Chir Belg* 1999; **99**: 147-50.
- 6) Shindo S, Tada Y, Kamiya K, Suzuki O, Kobayashi M, Iyori K, et al. Automatic sequential pneumatic tourniquet (pneumatic stocking) for distal bypass. *J Vasc Surg* 1995; **21**: 869-70.
- 7) Norgren L, Hiatt WR, Dormandy JA, Nehler MR, Harris KA, Fowkes FG. Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). *J Vasc Surg* 2007; **45** Suppl S: S5-67.
- 8) Criqui MH, Ninomiya JK, Wingard DL, Ji M, Fronek A. Progression of peripheral arterial disease predicts cardiovascular disease morbidity and mortality. *J Am Coll Cardiol* 2008; **52**: 1736-42.
- 9) Crawford RS, Cambria RP, Abularrage CJ, Conrad MF, Lancaster RT, Watkins MT, et al. Preoperative functional status predicts perioperative outcomes after infrainguinal bypass surgery. *J Vasc Surg* 2010; **51**: 351-9.
- 10) Abou-Zamzam AM Jr, Lee RW, Moneta GL, Taylor LM Jr, Porter JM. Functional outcome after infrainguinal bypass for limb salvage. *J Vasc Surg* 1997; **25**: 287-95.
- 11) Chung J, Bartelson BB, Hiatt WR, Peyton BD, McLafferty RB, Hopley CW, et al. Wound healing and functional outcomes after infrainguinal bypass with reversed saphenous vein for critical limb ischemia. *J Vasc Surg* 2006; **43**: 1183-90.
- 12) Sottiurai V, White JV. Extensive revascularization or primary amputation: which patients with critical limb ischemia should not be revascularized? *Semin Vasc Surg* 2007; **20**: 68-72.
- 13) Taylor SM, Kalbaugh CA, Blackhurst DW, Hamontree SE, Cull DL, Messich HS, et al. Preoperative clinical factors predict postoperative functional outcomes after major lower limb amputation: an analysis of 553 consecutive patients. *J Vasc Surg* 2005; **42**: 227-35.

► **Original Article** ◀

Indicators of Survival after Open Repair of Ruptured Abdominal Aortic Aneurysms and an Index for Predicting Aneurysmal Rupture Potential

Kohei Takahashi, MD, Daisuke Fukui, MD, PhD, Yuko Wada, MD, PhD, Takamitsu Terasaki, MD, Yoshinori Ohtsu, MD, PhD, Kazunori Komatsu, MD, Megumi Fuke, MD, Tamaki Takano, MD, PhD, and Jun Amano, MD, PhD

Background: The aims of this study were to assess variables associated with survival in patients undergoing ruptured abdominal aortic aneurysm (RAAA) repair and to develop an index other than the aneurysmal diameter to predict rupture potential.

Methods: This study included 43 consecutive patients who underwent open surgery for RAAAs.

Results: The mortality rate was 18.6% (8/43). The ratio between the maximum aneurysmal diameter and the length (along the central axis) from the aneurysmal neck to the point at which the diameter was three-fourth of the maximum aneurysmal diameter was used as an index to predict aneurysmal rupture potential. The index score was 2.7 ± 1.2 in the RAAA and 1.9 ± 0.9 in the EAAA ($p = 0.018$). For aneurysms of ≤ 6 -cm diameter, the index score was 3.0 ± 1.0 in the RAAA and 1.8 ± 0.9 in the EAAA ($p = 0.03$). All patients in the EAAA except one had an index score of < 2.3 and 6 of the 7 patients with RAAA had a score of > 3 .

Conclusions: The results suggest that patients with AAA having scores of > 3 are at high risk of rupture. This index would be useful for decision making regarding repair of AAA, especially in the borderline cases.

Key words: ruptured abdominal aortic aneurysm, emergency open repair; novel index score of rupture potential

INTRODUCTION

Despite the increased number of cases of elective abdominal aortic aneurysm (EAAA) repair, the number of patients with ruptured AAA (RAAA) has not significantly reduced in the past decade.¹⁾ Further, although the mortality rate following EAAA repair has steadily improved by about 1%–6%,²⁾ the mortality rate after

RAAA repair has not significantly changed in the last three decades and is still in the 30%–70% range.^{3,4)} Many factors, including age, comorbidity, medical condition, preoperative shock or hypotension, increased creatinine level, low hemoglobin or hematocrit level, and technical and postoperative complications, are considered predictors of death, but none of these correctly predict the outcome of patients with RAAA.^{5–7)}

The maximum transverse aneurysmal diameter has been the only criterion used to predict aneurysmal rupture potential in the last 40 years.⁸⁾ According to this criterion, aneurysms reaching 5–5.5 cm in diameter are generally recommended for repair.⁹⁾ However, there are many reports of rupture of aneurysms smaller than 5.5 cm in diameter; the estimated rupture rate of small aneurysms varies between 4.6% and 23%.¹⁰⁾ On the other hand, the incidental presentation of extremely large asymptom-

Department of Cardiovascular Surgery, Shinshu University School of Medicine, Matsumoto, Nagano, Japan

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Corresponding author: Kohei Takahashi, MD. Department of Surgery, Shinshu University School of Medicine, 3-1-1 Asahi, Matsumoto, Nagano 390-8621, Japan

Tel: +81-263-37-2657, Fax: +81-263-37-2721

E-mail: takahashi-kouhei@goo.jp

atic aneurysms demonstrates the potential for indolent rupture-free growth of some large aneurysms. Aneurysms of similar size are likely to have disparate growth rates; therefore, measurement of the maximum transverse aneurysmal diameter as the sole predictor of rupture potential is insufficient. Although this measure is the most reliable, another reliable clinical predictor of AAA rupture risk is necessary.^(11–16)

Recent studies have focused on AAA volume and vessel shape and tortuosity as potentially better predictors of AAA rupture risk,^(17–21) and the estimated maximum wall stress has received considerable attention in this regard.^(11, 12, 14, 15, 22) However, these criteria are not universally applicable because the imaging capabilities for quantifying these characteristics are still not available clinically. In addition, there are often cases of steep inclination of aneurysmal rise encountered during RAAA repair. In contrast, the maximum diameter criterion is widely applicable and currently used for decision-making purposes, importantly because the AAA size is the dominant consideration in the decision to intervene in asymptomatic patients. Therefore, another morphologic predictor that is suitable for practical application and which supports aneurysmal diameter for the estimation of AAA risk is required.

The aims of this study were to assess significant variables associated with survival in patients undergoing emergent RAAA repair and develop a predictive index of aneurysmal rupture potential.

METHODS

This study included 43 consecutive patients having RAAA without thoracic extension who presented at Shinshu University Hospital between January 2004 and June 2009. Data were collected retrospectively from the hospital information system, operating theater logbooks, and intensive care unit records. The diagnosis of rupture was confirmed by reviewing the preoperative axial computed tomography (CT) findings and description of intraoperative visualization of blood outside the aneurysmal wall, in the retroperitoneum, mesentery, or peritoneal cavity, for free rupture. The baseline characteristics of patients and intraoperative and postoperative variables were documented (**Table 1**). There were 35 (81%) men and 8 (19%) women (**Table 1**); the overall male-to-female ratio for all cases of RAAA was about 4 : 1. Most patients in the RAAA group were aged over 65 years (mean age = 75.5 ± 8.8 years), with the peak incidence at 75–80

years. There were 16 (37.2%) patients over the age of 80 years. Most patients (85%) were transferred from referring hospitals. Thirty-four patients had abdominal aortic aneurysmal rupture and nine had iliac arterial aneurysmal rupture.

The major operative complications were also recorded. Preoperative shock was defined as systolic blood pressure of < 80 mmHg. Postoperative renal insufficiency was defined as a serum creatinine level of > 2.0 mg/dl. Operative mortality was defined as death within 30 days of operation or in-hospital death if later than 30 days. Aneurysmal morphology, site, and type of rupture (open or closed), as well as intraoperative bleeding, were assessed. The aneurysms were classified into aortic aneurysmal rupture or iliac aneurysmal rupture. Further, extension of hematoma was grossly quantified with the Fitzgerald classification according to the anatomic compartments involved: type 1, the periaortic area; type 2, the retroperitoneal space but restricted to the caudal end of the renal artery; type 3, the retroperitoneal space and spread beyond the renal artery or into the intrapelvic space; type 4, intraperitoneal hemorrhage. The presence or absence of renal displacement and contrast agent extravasation were recorded as easily detectable indicators of hemorrhagic volume. To examine the statistical difference of the initial rising angle of the proximal side between RAAA and nonruptured AAA, patients with EAAA repair were randomly selected and matched to patients with RAAA according to the maximum aneurysmal diameter as the control group. All RAAA repairs were performed by open surgical procedure by cardiovascular surgeons.

To assess the initial rising angle of the proximal side of the aneurysm from horizontal centerline axis of the aorta as an index to estimate the aneurysmal expansion rate, the maximum transverse aneurysmal diameter (D) and the length along the central axis from the aneurysmal neck to the point at which the diameter was three-fourth of the maximum transverse aneurysmal diameter (L) were measured, using axial view of CT scan: the index is represented by $(3/4 \times D)/L$ (**Fig. 1**). To measure the precise diameter and length, we used only available 2.5–5.0 mm sliced enhanced CT with DICOM data, not to include hematoma in its diameter or the length. 25 patients out of 43 had these data and were available in this study. This is the reason, 25 patients out of 43 were analyzed in this study.

Table 1 Baseline characteristics of patients who underwent open repair of ruptured abdominal aortic aneurysms

Variable	Value
Demographics	
Age (yr)	75.5 ± 8.8
Female gender	18.6 (8)
History of COPD	7.0 (3)
History of CVA	37.2 (16)
History of CAD	23.2 (10)
History of DM	18.6 (8)
History of PVD	7.0 (3)
History of hypertension	83.7 (36)
History of CRF	1.6 (5)
History of hyperlipidemia	27.9 (12)
History of hemodialysis	0.0 (0)
Current smoking	20.9 (9)
Preoperative characteristics	
Prior aortic reconstruction	9.3 (4)
Distance to hospital (km)	25.3 ± 24.0
Transfer by air	11.6 (5)
Iliac artery aneurysmal ruptur	20.9 (9)
Free rupture	14.0 (6)
SBP < 80 mmHg	79.1 (34)
SBP	90.8 ± 29.8
Shock index (HR/SBP)	1.16 ± 0.7
ER-to-OP start time (min)	96 ± 56
CPR	0.0 (0)
Blood chemistry	
Mean hemoglobin level (g/dl)	9.5 ± 3.5
Mean platelet count (× 10 ⁴ cells)	14.3 ± 6.8
Intraoperative variables	
Proximal aortic clamp site	
Supraceliac	11.6 (5)
Suprarenal	27.9 (12)
Infrarenal	60.5 (26)
Intrathoracic	0.0 (0)
Clamp time (min)*	
Supraceliac	78.5 ± 58.7 (5)
Suprarenal	84.3 ± 24.8 (12)
Infrarenal	93 ± 16 (26)
Lowest BP (mmHg)	47.9 ± 17.4
IMA reconstruction	46.5 (20)
Postoperative variables	
Renal failure requiring hemodialysis	4.7 (2)
Renal failure (Cr level > 2 mg/dl)	34.9 (15)
Myocardial infarction	0.0 (0)
Tracheostomy	4.7 (2)
Stroke	2.3 (1)
Intestinal ischemia	0.0 (0)
Failure to close abdomen	11.6 (5)

The data are the percentage (n) or the mean ± standard deviation of 43 patients.

*The values in parentheses are the number of cases.

COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; CAD, coronary artery disease; DM, diabetes mellitus; PVD, peripheral vascular disease; CRF, chronic renal failure; SBP, systolic blood pressure; HR, heart rate; ER, emergency room; OP, operation; CPR, cardiopulmonary resuscitation; IMA, inferior mesenteric artery

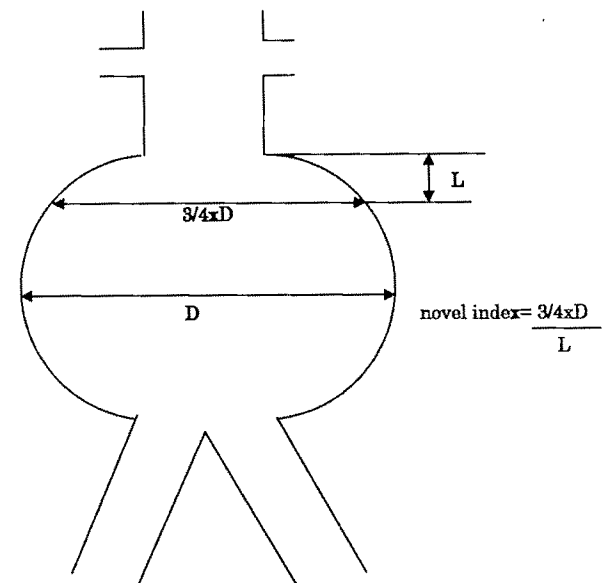


Fig. 1 Schematic of a representative abdominal aortic aneurysm (AAA) indicating the index for predicting aneurysmal rupture potential. The index is defined as $(3/4 \times D)/L$, where D is the maximum AAA diameter (transversally) and L is the length (measured along the central axis) of the AAA from the neck to the point at which the diameter is $3/4 \times D$.

Statistical Analysis

Continuous variables are summarized as the mean and standard deviation (SD), and categorical variables are summarized as the number of cases and percentage. The Mann-Whitney *U*-test, unpaired Student's *t*-test, 2×2 chi-square test, Fisher exact probability test, and Yates chi-square test were used in the univariate analysis to identify demographic, clinical, and postoperative factors associated with operative mortality and determine differences in the index scores between RAAA and EAAA. All analyses were performed with SAS version 9.1 under the alpha level of 0.05 (SAS Institute, Inc., Cary, NC) and EXCEL (Microsoft Co. Ltd.).

RESULTS

The mean diameter of the ruptured AAA was 7.24 ± 1.4 . The mode of transportation was by air in five cases (11.6%) and by road in 39 cases (88.4%). Six patients (14%) presented with free rupture. All patients complained of transient or continuous pain. Aortoenteric fistulae were noted in two patients. Nine patients presented with ruptured iliac aneurysms. Systolic blood pressure

Table 2 Correlation between IMA reconstruction and IIA sacrifice

Procedure	N
Unilateral IIA sacrificed	7
IMA reconstruction	5 (71.4%)
Bilateral IIAs sacrificed	5
IMA reconstruction	4 (80.0%)
Bilateral IIAs preserved	31
IMA reconstruction	12 (38.7%)

IMA, inferior mesenteric artery; IIA, internal iliac artery

Table 3 Univariate analysis of continuous variables

Variable	Survivors	Nonsurvivors	p
Age (yr)	75.3	76.5	0.481
Serum Cr level (mg/dl)	1.41	1.19	0.343
Preoperative Hb level (g/dl)	9.6	9.0	0.41
Preoperative platelet count ($\times 10^3$ cells)	15.5	9.3	0.0089
Preoperative SBP (mmHg)	94.3	76.4	0.064
Preoperative shock index (HR/SBP)	1.1	1.5	0.013
Intraoperative lowest BP (mmHg)	50.8	36.3	0.018
Intraoperative blood loss (g)	3940	11050	0.035

Cr, creatinine; Hb, hemoglobin; SBP, systolic blood pressure; HR, heart rate

of < 80 mmHg (preoperative shock status) was registered in 34 cases (79%). Most surgeries were started within 96 ± 58 min from hospital arrival; especially, in the five cases of severe shock (systolic blood pressure < 60 mmHg), the operation was begun more quickly (62.6 ± 23 min). A midline transperitoneal approach was used in all patients. Proximal aorta clamping was achieved primarily at the infrarenal site in 26 patients (60.5%). In the case of 17 other patients (39.5%) with critical hypotension or difficult identification of the infrarenal aortic neck, the initial aortic clamp was placed above the renal arteries, mostly at the supraceliac aorta (5 cases, 11.6%). A supra celiac clamp was temporarily placed before the infrarenal control. Thoracotomy and descending aortic clamping were not performed to shorten the duration of supraceliac clamping.

The inferior mesenteric artery (IMA) was reconstructed in five of seven patients whose unilateral internal iliac arteries (IIAs) were sacrificed (**Table 2**). The IMA was reconstructed in four of five cases whose bilateral IIAs were sacrificed. Further, the IMA was reconstructed in 12 of 31 patients whose bilateral IIAs were preserved. The mean operative time was 282 ± 84 min.

The overall in-hospital mortality rate was 18.6% (8/43). The intraoperative mortality rate was 7.0% (3/43), and deaths mainly resulted from continued hemorrhage and irreversible shock in these cases.

The preoperative variables associated with death after RAAA repair are listed in **Table 3** and **Table 4**. Of the continuous variables, the preoperative platelet count, preoperative shock index, intraoperative blood loss, and intraoperative lowest systolic blood pressure were significantly associated with perioperative death. Further, of the categorical variables, the rupture type (free or closed), extension of hematoma (Fitzgerald classification), preoperative general condition (American Society of Anesthesiologists classification), and extravasation of contrast agent during CT scan were significantly associated with perioperative death.

The most common postoperative complications among the 40 patients who survived at least one day after surgery were respiratory failure requiring mechanical support over 72 h (7 patients, 17.5%), pneumonia (5 patients, 12%), and renal failure requiring dialysis (3 patients, 7%). Three patients died because of multiple organ failure within 15 postoperative days. One patient made satisfactory

Table 4 Univariate analysis of categoric variables

Variable	Survivors	Nonsurvivors	<i>p</i>
Open rupture	2	4	0.009
Closed rupture	33	4	
Fitzgerald classification			0.048
Class 1	2	0	
Class 2	7	0	
Class 3	21	2	
Class 4	1	3	
ASA classification			0.001
Class 1	0	0	
Class 2	0	0	
Class 3	0	0	
Class 4	31	2	
Class 5	4	6	
Extravasation of contrast agent in CT scan	4	2	0.015
No extravasation	18	0	
Renal dislocation in CT scan	17	3	1.0
No renal dislocation	12	2	
Preoperative catecholamine use	5	3	0.137
No catecholamine	27	4	
Preoperative shock status	24	8	0.16
No shock	9	0	
Supraceliac clamp	3	2	0.312
Suprarenal clamp	8	4	
Infrarenal clamp	24	2	
No IIA sacrificed	23	6	
Unilateral IIA sacrificed	5	2	
Bilateral IIAs sacrificed	5	0	0.856
AAA rupture	24	8	
Iliac artery aneurysmal rupture	9	0	0.164

ASA, American Society of Anesthesiologists; IIA, internal iliac artery; AAA, abdominal aortic aneurysm

progress after the operation but developed graft infection and underwent graft excision and anti-anatomical reconstruction 2 months after the operation; he died of rupture of a thoracoabdominal aortic aneurysm. Three patients underwent a second laparotomy for intestinal ischemia, but there were no cases of severe intestinal ischemia requiring bowel resection. No patient developed postoperative spinal palsy.

The novel index score was 2.7 ± 1.2 in the RAAA cases and 1.9 ± 0.9 in the EAAA cases (Fig. 2). Especially, for aneurysms of ≤ 6 -cm diameter, the index score was 3.0 ± 1.0 in the RAAA cases and 1.8 ± 0.9 in the EAAA cases (Fig. 3). There were significant differences between the groups irrespective of the aneurysmal diameter. All patients with RAAA except one had index scores of > 3.0 , and all patients in the EAAA group

except one had scores of < 2.3 . There was no significant difference between the groups in terms of aneurysmal diameter (Fig. 4).

DISCUSSION

The mortality rate of ruptured aneurysms is remarkably high. With the exception of a few series,^{23, 24)} it has been reported as ranging from 30% to $> 70\%$.⁴⁾ If patients who died at home or during transport to a hospital are included, the mortality rate approaches 90%.^{25, 26)} This excessively high operative mortality rate can be explained by the facts that patient selection is usually impossible, and the majority have already suffered the consequences of hypovolemic shock at admission. Johansen et al.⁴⁾ demonstrated a mortality rate of 70% in 186 patients with

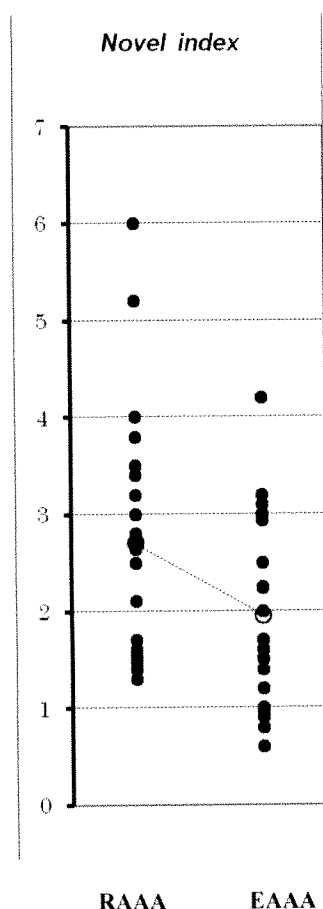


Fig. 2 Comparison of the index scores of the ruptured abdominal aortic aneurysm (RAAA) and elective abdominal aortic aneurysm (EAAA) groups. The index score was 2.7 ± 1.2 in the RAAA cases and 1.9 ± 0.9 in the EAAA cases. There were significant differences between the groups ($p = 0.018$).

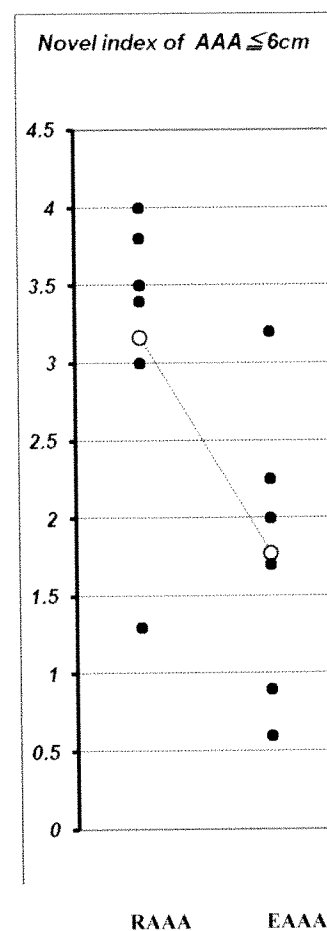


Fig. 3 Comparison of the index scores of the ruptured abdominal aortic aneurysm (RAAA) and elective abdominal aortic aneurysm (EAAA) groups for aneurysms of ≤ 6 -cm diameter. The index score was 3.0 ± 1.0 in the RAAA cases and 1.8 ± 0.9 in the EAAA cases. There were significant differences in this series ($p = 0.03$).

RAAA treated at a single hospital; this survival rate was measured despite specialized prehospital management and transport, short emergency department diagnostic evaluation, aneurysmal repair by an operating vascular surgery team, and sophisticated postoperative care.

Considering the high mortality rate combined with the associated high hospital costs, Hardmann et al.²⁷⁾ suggested that certain preoperative variables (preoperative cardiac arrest, age > 80 years, male gender, persistent preoperative hypotension despite aggressive crystalloid and blood replacement, admission hematocrit < 25 , transfusion requirements exceeding 15 units) should be used to identify patients most likely to die, and would, therefore, be best treated without surgery. This approach may

have some justification in this age of cost-effective therapy, but it also has significant ethical and legal implications. In the present study, there were no patients requiring cardiopulmonary resuscitation because the emergency staff administered the appropriate critical and intensive care, and anesthesiologists and the operating room staff coordinated to start the operation quickly. These factors were considered to be the reason for the good survival rate. Further, comparison of the mean age between survivors and nonsurvivors did not yield a statistically significant difference; surgical repair of RAAA was performed in all patients regardless of age. However, the number of preoperative deaths in the same area could not be confirmed. Aortic clamping under thoracotomy is

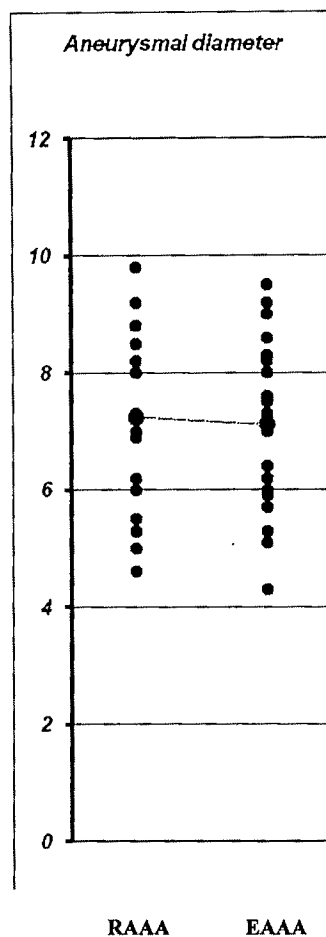


Fig. 4 Comparison of aneurysmal diameters in ruptured abdominal aortic aneurysm (RAAA) and elective abdominal aortic aneurysm (EAAA) groups. The diameter was 5.3 ± 0.5 in the RAAA cases and 5.4 ± 0.6 in the EAAA cases. There were no significant differences between the groups.

considered to be necessary especially in case of severe shock. However, supraceliac clamp under thoracotomy causes severe operative complications, intestinal ischemia, and paraplegia. Therefore, in this study, the supraceliac clamping time was maintained as short as possible, without thoracotomy.

Johansen et al.⁴⁾ suggested that the decision to deny operative treatment to a patient with RAAA should be made while considering each patient individually and can be justified only in those cases with poor quality of life due to a precarious general medical status or mental condition. Rather than using predictive variables to identify patients who will not survive, several studies, including this study, have been conducted to determine the surgical

tactics and anesthesiological procedures that can improve the survival rate and identify patients in whom preoperative conditions and other clinical factors make conventional surgical repair inopportune. Although several authors noted higher mortality rates among elderly patients,^{6, 25, 28, 29)} advanced age was not found to be a significant predictor of survival in this study. Once elderly patients have survived the operation, they can enjoy a long life expectancy, similar to their contemporaries in the general population.^{28, 29)} Thus, it is reasonable to consider that physiologic age is more relevant than chronological age even if older patients are exposed to increased surgical risk in the case of aneurysmal rupture. Of the 43 patients who underwent open RAAA repair in this study, 35 (81.4%) survived surgery. The fact that 16 of the 43 patients (37.2%) were older than 80 years justifies our opinion regarding age. Age may be considered an indirect marker of physiologic status.

In this study, eight significant risk factors were identified in the univariate analysis. Of the continuous variables, preoperative shock index, preoperative platelet count, intraoperative lowest systolic blood pressure, and intraoperative blood loss were predictive of perioperative death. The change in these variables was affected by the amount of bleeding. Of all the categorical variables, rupture type (free or closed), extension of hematoma, preoperative general condition, and extravasation of contrast agent during CT scan were significantly associated with perioperative death. The presence or absence of contrast agent extravasation is an easily detectable indicator of hemorrhagic volume. The significant categorical variables except the preoperative general condition also reflect the amount of bleeding.

As a general rule, the IMA was reconstructed to prevent intestinal ischemia unless IMA good pulsation was confirmed. With this operative policy, no severe intestinal ischemia requiring bowel resection or spinal palsy was observed postoperatively. A previous paper reported that about 3%–15% of patients develop intestinal ischemia requiring intestinal resection as a complication of RAAA repair. Some patients have intestinal ischemia after RAAA repair in spite of IMA reconstruction. In this series, a second exploratory laparotomy was performed in the three IMA-reconstructed cases to examine intestinal ischemia. Fortunately, there was no case of intestinal ischemia requiring resection. In addition, among patients with aortoenteric fistula, one was saved, by surgical repair with extra-anatomical bypass, and discharged as ambulatory on postoperative day 42. Another

patient with aortoenteric fistula was operated with anatomic reconstruction, but he died on postoperative day 1 because of shock.

In this study, we designed an easy and useful predictor for rupture suitable for practical, clinical use. Giannoglou et al.³⁰⁾ suggested that the mean AAA curvature may be a better predictor of AAA rupture risk, although they implemented linearly elastic material properties. We often experience such cases which have a steep, inclinational initial rise of aneurysms in RAAA surgical repair.

We attempted to quantify the rising angle of proximal AAA, ruptured AAA, and elective repaired AAA (EAAA), and examined the correlation between rupture potential and novel quantitative rising angle novel index. In order to assess the rising angle of proximal aneurysm arising from horizontal centerline axis of the aorta, we measured maximum transverse diameter of AAA (D) and the length of centerline axis from aneurismal neck to the maximum point of AAA using axial view of CT scan, because only an axial view of CT date from reference hospitals were available in many cases. Next, we calculated $3/4 \times D$ and measured the length of centerline axis from aneurismal neck to the point of diameter of $3/4 \times D$ (L) (**Fig. 1**). The novel index of RAAA potential was defined $(3/4 \times D)/L$. AAA consists of a steeply sloped portion and a gently sloped portion. If only the maximum transverse diameter is used in this index, both gently and steeply sloped portion will be assessed. Therefore, to include only steeply sloped portion, the length to three-fourth of the maximum diameter was included. So it was considered that estimation of $(3/4 \times D)/L$ might be able to assess steeply sloped portion more than estimation of D/L , and we could get these results in this report. We calculated these indexes of 25 RAAA cases and 24 elective AAA cases (EAAA) as a control group. Diameter between RAAA and EAAA has no difference (**Fig. 4**). The index was 2.7 ± 1.2 in RAAA cases, 1.9 ± 0.9 in EAAA cases. Especially, in smaller AAA cases under 6-cm diameter, the index was 3.0 ± 1.0 in RAAA cases and 1.8 ± 0.9 in EAAA cases (**Figs. 2 and 3**). There was a significant difference between the index of RAAA and EAAA, statistically. There was more remarkable difference in smaller AAA cases under 6 cm (**Fig. 3**). In this figure, all RAAA cases despite one case revealed more than 3 index. Additionally, all EAAA cases despite one revealed less than 2.3 index. These results suggest that the AAA cases whose novel indexes were revealed as over 3 may be a high risk group for rupture even if its diameter is under 6-cm diameter. On the other hand, in

cases whose indexes were less than 2, a traditional maximum diameter of AAA may be a more reliable criterion with those aneurysms that reach 5–5.5 cm diameter, generally recommended for repair.

In conclusion, index scores of > 3 may be good predictors of the risk of AAA rupture and patients with these scores should be considered at high risk. This index would be useful to clinicians for decision making regarding surgical repair of AAA, especially in the case of borderline lesions (≤ 6 -cm diameter).

REFERENCES

- 1) Wanhainen A, Bylund N, Bjorek M. Outcome after abdominal aortic aneurysm repair in Sweden 1994–2005. *Br J Surg* 2008; **95**: 564–70.
- 2) Antonello M, Frigatti P, Maturi C, Lepidi S, Noventa F, Pittoni G, et al. Open repair for ruptured abdominal aortic aneurysm: is it possible to predict survival? *Ann Vasc Surg* 2009; **23**: 159–66.
- 3) Johnston KW. Ruptured abdominal aortic aneurysm: six-year follow-up results of a multicenter prospective study. Canadian Society for Vascular Surgery Aneurysm Study Group. *J Vasc Surg*. 1994; **19**: 888–900.
- 4) J Johansen K, Kohler TR, Nicholls SC, Zierler RE, Clowes AW, Kazmers A. Ruptured abdominal aortic aneurysm: the Harborview experience. *J Vasc Surg* 1991; **13**: 240–5.
- 5) Harris LM, Faggioli GL, Fiedler R, Curl GR, Ricotta JJ. Ruptured abdominal aortic aneurysms: factors affecting mortality rates. *J Vasc Surg* 1991; **14**: 812–20.
- 6) Halpern VJ, Kline RG, D'Angelo AJ, Cohen JR. Factors that affect the survival rate of patients with ruptured abdominal aortic aneurysms. *J Vasc Surg* 1997; **26**: 939–48.
- 7) Koskas F, Kieffer E. Surgery for ruptured abdominal aortic aneurysm: early and late results of a prospective study by the AURC in 1989. *Ann Vasc Surg*. 1997; **11**: 90–9.
- 8) Guirgis EM, Barber GG. The natural history of abdominal aortic aneurysms. *Am J Surg* 1991; **162**: 481–3.
- 9) Pappu S, Dardik A, Tagare H, Gusberg RJ. Beyond fusiform and saccular: a novel quantitative tortuosity index may help classify aneurysm shape and predict aneurysm rupture potential. *Ann Vasc Surg* 2008; **22**: 88–97.
- 10) Mortality results for randomised controlled trial of early elective surgery or ultrasonographic surveillance for small abdominal aortic aneurysms. The UK Small Aneurysm Trial Participants. *Lancet* 1998; **352**: 1649–55.
- 11) Fillinger MF, Marra SP, Raghavan ML, Kennedy FE. Prediction of rupture risk in abdominal aortic aneurysm during observation: wall stress versus diameter. *J*

- Vasc Surg 2003; **37**: 724-32.
- 12) Fillinger MF, Raghavan ML, Marra SP, Cronenwett JL, Kennedy FE. In vivo analysis of mechanical wall stress and abdominal aortic aneurysm rupture risk. *J Vasc Surg* 2002; **36**: 589-97.
 - 13) Wang DH, Makaroun MS, Webster MW, Vorp DA. Effect of intraluminal thrombus on wall stress in patient-specific models of abdominal aortic aneurysms. *J Vasc Surg* 2002; **36**: 598-604.
 - 14) Raghavan ML, Vorp DA, Federle MP, Makaroun MS, Webster MW. Wall stress distribution on three-dimensionally reconstructed models of human abdominal aortic aneurysm. *J Vasc Surg* 2000; **31**: 760-9.
 - 15) Vorp DA, Raghavan ML, Webster MW. Mechanical wall stress in abdominal aortic aneurysm: influence of diameter and asymmetry. *J Vasc Surg* 1998; **27**: 632-9.
 - 16) Scotti CM, Shkolnik AD, Muluk SC, Finol EA. Fluid-structure interaction in abdominal aortic aneurysms: effects of asymmetry and wall thickness. *Biomed Eng Online* 2005; **4**: 64.
 - 17) Shahcheraghi N, Dwyer HA, Cheer AY, Barakat AI, Rutaganira T. Unsteady and three-dimensional simulation of blood flow in the human aortic arch. *J Biomech Eng* 2002; **124**: 378-87.
 - 18) Di Martino ES, Guadagni G, Fumero A, Ballerini G, Spirito R, Biglioli P, et al. Fluid-structure interaction within realistic three-dimensional models of the aneurysmatic aorta as a guidance to assess the risk of rupture of the aneurysm. *Med Eng Phys* 2001; **23**: 647-55.
 - 19) Elger DF, Blackketter DM, Budwig RS, Johansen KH. The influence of shape on the stresses in model abdominal aortic aneurysms. *J Biomech Eng* 1996; **118**: 326-32.
 - 20) Finol EA, Keyhani K, Amon SH. The effect of asymmetry in abdominal aortic aneurysms under physiologically realistic pulsatile flow conditions. *J Biomech Eng* 2003; **125**: 207-17.
 - 21) Taylor TW, Yamaguchi T. Three-dimensional simulation of blood flow in an abdominal aortic aneurysm—steady and unsteady flow cases. *J Biomech Eng* 1994; **116**: 89-97.
 - 22) Fillinger MF, Racusin J, Baker RK, Cronenwett JL, Teutelink A, Schermerhorn ML, et al. Anatomic characteristics of ruptured abdominal aortic aneurysm on conventional CT scans: implications for rupture risk. *J Vasc Surg* 2004; **39**: 1243-52.
 - 23) Crawford ES. Ruptured abdominal aortic aneurysm: an editorial. *J Vasc Surg* 1991; **13**: 348-50.
 - 24) Lawrie GM, Crawford ES, Morris GC Jr, Howell JF. Progress in the treatment of ruptured abdominal aortic aneurysm. *World J Surg* 1980; **4**: 653-60.
 - 25) Johansson G, Swedenborg J. Ruptured abdominal aortic aneurysms: a study of incidence and mortality. *Br J Surg* 1986; **73**: 101-3.
 - 26) Budd JS, Finch DR, Carter PG. A study of the mortality from ruptured abdominal aneurysms in a district community. *Eur J Vasc Surg* 1989; **3**: 351-4.
 - 27) Hardman DT, Fisher CM, Patel MI, Neale M, Chambers J, Lane R, et al. Ruptured abdominal aortic aneurysms: who should be offered surgery? *J Vasc Surg* 1996; **23**: 123-9.
 - 28) Kazmers A, Perkins AJ, Jacobs LA. Outcomes after abdominal aortic aneurysm repair in those ≥ 80 years of age: recent Veterans Affairs experience. *Ann Vasc Surg* 1998; **12**: 106-12.
 - 29) Glock Y, Smile E, Dalous P, Roux D, Fournial G, Cerene A, et al. Abdominal aortic aneurysmectomy in octogenarian patients. *J Cardiovasc Surg (Torino)* 1990; **31**: 71-6.
 - 30) Giannoglou G, Giannakoulas G, Soulis J, Chatzizisis Y, Perdikides T, Melas N, et al. Predicting the risk of rupture of abdominal aortic aneurysms by utilizing various geometrical parameters: revisiting the diameter criterion. *Angiology* 2006; **57**: 487-94.

► **Original Article** ◀

Early Outcomes of Endovascular Aneurysm Repair for Abdominal Aortic Aneurysm: First Preliminary Report of National Hospital Organization Network Study in Japan

Nobuhiro Handa, MD, Toshihiro Onohara, MD, Keiichi Akaiwa, MD, Jyunichi Kei, MD, Minoru Okamoto, MD, Tsuyoshi Yamamoto, MD, Yasushi Shimoe, MD, Mikizou Nakai, MD, Masahiro Okada, MD, Toshiki Takahashi, MD, Hitoshi Suhara, MD, Fuminari Kasashima, MD, Masamitsu Endo, MD, Takeshi Nishina, MD, Tadashi Furuyama, MD, Yoichirou Ueno, MD,

National Hospital Organization Network Study Group in Japan for Abdominal Aortic Aneurysm

Objective: Patients and Methods: In order to assess the early outcomes of endovascular aneurysm repair (EVAR) for abdominal aortic aneurysm (AAA) in the Japanese population, a total of 183 patients who had EVAR at eight medical centers of the National Hospital Organization were retrospectively reviewed and registered. The mean number of registered cases in each center was 23 ± 17 (4–50 cases). Patient characteristics were male sex, 84%; mean age, 77 years; age ≥ 80 years, 40%.

Results: In-hospital mortality was one case (0.5%). Endoleaks were observed at the end of the procedure in 35 patients (19%: type I: $n = 4$, II: $n = 22$, III, $n = 3$, IV: $n = 6$). Early morbidity included delayed wound healing or infection ($n = 7$), deterioration of renal dysfunction ($n = 3$), stroke ($n = 2$), postoperative bleeding ($n = 2$), gastrointestinal complications ($n = 2$), and peripheral thromboembolism ($n = 2$). Eleven late deaths included one of unknown cause and six cardiovascular causes at a mean follow up of 1.0 year. Survival rates of freedom from all causes of death and from aneurysm-related death at one year were $95.4\% \pm 1.7\%$ and $99.5\% \pm 0.5\%$, respectively.

Interpretation: Although registered patients carry a variety of risks, early outcomes were satisfactory. EVAR is an acceptable alternative treatment modality for treating AAA.

Key words: endovascular aneurysm repair, multicenter study, abdominal aortic aneurysm

INTRODUCTION

From 2004 to 2006, approximately seven to eight thousand cases of infra-renal abdominal aortic aneurysm (AAA) had been repaired annually in Japan.¹⁾ The results of open abdominal repair in a nationwide survey by the Japanese Society for Vascular Surgery showed excellent

results of early mortality of 2%–3% in whole patients and 0.6%–0.9% in unruptured cases.¹⁾ Recent advances of endovascular aneurysm repair (EVAR) for AAA provide a less invasive approach for patients who are ineligible or carry high risks for open abdominal surgery. The advantage and the disadvantage of EVAR in comparison with open abdominal repair have been disputed in many articles outside Japan.^{2–6)} Three prospective randomized trials have been reported which suggested that endovascular approach was superior to open abdominal repair for unruptured AAA in early results, and was not inferior to in mid term results.^{2–4)} It was noted, however, that their reported mortality rates of the open surgical arm ranged from 3.0% to 4.7%, and the EVAR arm ranged from 0.5% to 1.7%. There is criticism among Japanese

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Affiliations of participants in National Hospital Organization Network Study Group in Japan for Abdominal Aortic Aneurysm are listed in Appendix.
Corresponding author: Nobuhiro Handa, MD, Department of Cardiovascular Surgery, Nagara Medical Center, 1300-7, Nagara, Gifu, Gifu 502-8558, Japan
Tel: +81-58-232-7755, Fax: +81-58-295-0077
E-mail: handa-kegh@umin.ac.jp

vascular surgeons that reported mortalities of EVAR outside Japan are higher than that of open surgical cases in Japan. Unfortunately, the introduction of such products and devices into Japan for endovascular repair of AAA was delayed until July 2007, when they were approved by the Ministry of Labor and Welfare of Japan. As a result, early results of EVAR by a multi-center cooperative study have not been published in the Japanese population at the moment. In the present study, eight centers of National Hospital Organization (NHO) joined to form registration of AAA cases retrospectively. The present interim goal of the study is to report early results of EVAR in Japan by analyzing registered cases collected by NHO Network Study Group for AAA.

METHODS

The study was a retrospective observational study to review EVAR cases and to form registration at eight participating centers. The study was approved by the human rights ethical committee, and institutional review boards at each participating center. Progress of the study was assessed annually, and an extension of the study was approved by the central human rights ethical committee of NHO. All participating institutions displayed the notice that they joined the NHO network study of AAA in the center according to the ethical guidelines for epidemiological research published by the Ministry of Education, Culture, Sports, Science and Technology, and the Ministry of Health, Labor and Welfare in Japan.⁷⁾

Patients and registration

Eligible patients who had endovascular aneurysm repair for abdominal and/or iliac artery aneurysm were registered retrospectively. General indications for treating AAA are as follows: maximum external diameter ≥ 5 cm or 4–5 cm with rapid enlargement, or a saccular morphology, which carries a high risk of rupture. Each patient had a preoperative examination including a multi-detector computed tomography (CT) examination according to the requirements in each participating center. The choice of treatment modality between EVAR and open abdominal repair depended upon the decision making by surgeons and endovascular therapists. Only endovascular systems approved by the Ministry and Welfare of Japan were included in the study. Patients who were treated with a homemade stent graft were excluded from the analysis. A total of 110 variables consisting of preoperative, intraoperative and postoperative variables were collected.

Parameters were selected, based on the 10 risk scores previously published for predicting risks of open abdominal repair of AAA.⁸⁾ After anonymization in a linkable fashion, all databases at 8 centers were connected into one large database at Nagara Medical Center. A total of 183 patients were registered at the end of March 2010.

Outcome measures

The primary outcome measure was in-hospital mortality. Secondary outcome measures included early morbidities, and intermediate term results. Survival rates of freedom from all causes of death, from aneurysm-related death and other events, were calculated with Kaplan-Meier survival analysis. Details of treatments were described such as procedure time, volume of blood transfusion, and process of recovery including hours of respiratory management, intensive care unit stay (ICU stay), procedure failure requiring additional procedure during the same hospitalization, and readmission. Preoperative patient characteristics and intra-operative and postoperative factors are described in **Table 1**, including preoperative physiological status of American Society of Anesthesiology (ASA),⁹⁾ and both preoperative and postoperative Physical Performance Indices (PPI).¹⁰⁾ The ASA classes are as follows; Class 1 = normal healthy, Class 2 = mild systemic disease, Class 3 = severe systemic disease that is not incapacitating, Class 4 = incapacitating systemic disease that is a constant threat to life. Class 5 = moribund, not expected to survive for 24 hours with or without surgery. PPI is defined as follows: Grade 0 = fully active and able to perform all predisease activities without restriction, Grade 1 = restricted strenuous physical activity but ambulatory and able to perform work of a light or sedentary, Grade 2 = ambulatory and capable of only limited self-care but unable to perform any work activities for up to or more than 50% of waking hours. Grade 3 = capable of limited self-care and confined to bed or chair for more than 50% of waking hours. Grade 4 = completely disabled, unable to perform any self-care and totally confined to bed or chair.

RESULTS

Patient characteristics and preoperative condition

Patient characteristics are detailed in **Table 1**. Patients who had EVAR were predominantly of the male gender and were old (male sex: 84%; mean age, 77 years old). About 40% of patients were more than or equal to 80 years old. Distribution of AAA size was shown in **Table 1**

Table 1 Patient characteristics

Age (mean $\pm$ standard deviation), years	77 $\pm$ 9
Age distribution	
Age $\geq$ 80 year old	73 (40%)
79 $\geq$ age $\geq$ 70	84 (46%)
69 $\geq$ age $\geq$ 60	24 (13%)
59 $\geq$ age	2 (1%)
Gender (male sex)	154 (84%)
Distribution of AAA size (mm)	51.3 $\pm$ 9.4
$\geq$ 60 mm	37 (20%)
60 mm > diameter $\geq$ 50 mm	69 (38%)
50 mm > diameter $\geq$ 40 mm	66 (36%)
40 mm > diameter	11 (6%)
BMI $\geq$ 30	3 (2%)
BMI $\geq$ 25	49 (27%)
Current smoker	17 (9%)
Ex-smoker	81 (44%)
Hypertension	152 (83%)
Diabetes mellitus	28 (15%)
On dialysis	4 (2%)
Preoperative renal dysfunction (Cr $\geq$ 1.5) without dialysis	13 (7%)
Liver cirrhosis	3 (2%)
Coronary artery disease	65 (36%)
Myocardial ischemia	32 (17%)
Stroke	46 (25%)
with residual neurological deficit	12 (7%)
without neurological deficit	34 (19%)
NYHA class II	34 (19%)
NYHA class III	5 (3%)
NYHA class IV	0 (0%)
Previous permanent pacemaker placement	5 (3%)
Preoperative steroid use	5 (3%)
COPD on inhaled drug therapy	10 (5%)
FEV1.0% < 70%	67 (37%)
Preoperative vital capacity (< 70% of normal)	98 (54%)
History of abdominal surgery	49 (27%)
Once	37 (19%)
Twice or more	12 (8%)

as well. The mean diameter was 51.3 $\pm$ 9.4mm. Eleven patients who had an AAA size less than 40mm were indicated for EVAR because of either a saccular morphology of aneurysm or their location, mainly in common iliac artery. Co-morbid conditions included coronary artery disease (36%), induced myocardial ischemia (17%), history of stroke (25%), and history of abdominal surgery (27%). Preoperative patient condition for procedure and anesthesia was graded by American Society of Anesthesiology, which showed concomitant mild systemic disease (55%), severe systemic disease (21%) and life threatening condition (2%). Physical performance index as an indica-

tor of physical activity before surgery showed that about 50% of folks showed limited physical activity to some degree and that 20% were moderately or severely disturbed as daily activity (**Fig. 1**).

Details of EVAR procedure and postoperative recovery

Devices used for EVAR were as follows: COOK Zenith AAA endoprosthesis 96 cases (52%), Gore Tex Excluder 76 case (46%), and Endologix PowerLink 11cases (6%). Twenty eight percent of cases were beyond the manufacture's recommendation for use. Causes beyond manufacture's recommendation were detailed in **Table 2**. It was noted that angulated neck and short distal landing zone were the two major reasons. Duration of procedure time was 163 $\pm$ 64 minutes. Average transfusion volume of banked red blood cell was 94 $\pm$ 321 ml. Recovery from procedure was fast and smooth. Mean hours of mechanical ventilation support was 0.3 $\pm$ 1.3 hours only. Mean duration from the end of the procedure to start meal and walking were 1.4 $\pm$ 2.8 days and 1.3 $\pm$ 1.7 days respectively.

Early results

Early mortality and morbidity are shown in **Table 3**. In-hospital mortality was one (0.5%). Endoleaks were observed at the end of the procedure in 35 (19%) patients, (type I: n = 4, type II: n = 22, type III: n = 3, type IV: n = 6). Early morbidity included delayed wound healing or infection, the most frequently observed complication in the study. In addition, three patients required transient dialysis after the procedure. It was noted that two patients each had stroke, re-exploration for bleeding, acute ischemia of the limb and a gastrointestinal complication. Five patients (2.7%) were readmitted within 30 days after EVAR for various reasons. Causes for readmission included acute type B dissection, respiratory insufficiency due to interstitial pneumonia, infection of urinary tract and so on.

Intermediate term results

The mean duration of follow-up was only 1.0 $\pm$ 0.7 years. Eleven patients died at follow-up. No obvious aneurysm-related death was reported. However, six patients died due to cardiovascular causes (acute myocardial infarction, 2 cases; congestive heart failure, 2 cases; rupture of cerebral aneurysm, 2 cases). Two patients died of malignant neoplasm. One patient had interstitial pneumonitis, which deteriorated and developed into respiratory failure, resulting in death. One patient died of an unknown cause, which was included as an aneurysm-related death.

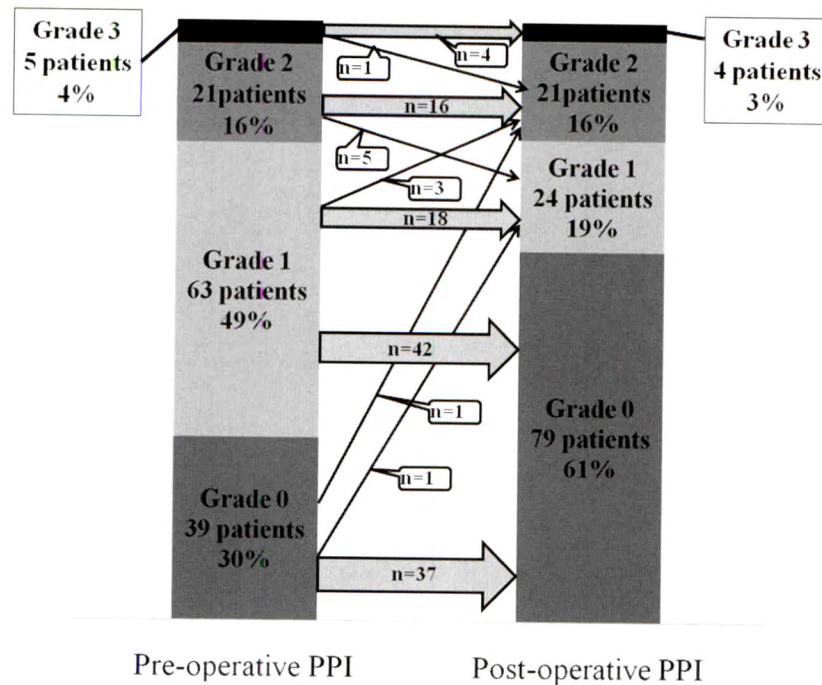


Fig. 1 Preoperative and postoperative physical performance index (PPI) of 129 patients whose data of both preoperative and postoperative grades were available.

Table 2 Causes beyond manufacture's recommendation

Angulated neck	13
Short distal landing zone	13
Short neck	10
Access problem	7
Circumferential thrombus	4
Narrow terminal aorta	3
Others	5

Table 3 Early results

In-hospital mortality	1 (0.5%)
Endoleak	35 (19%)
Type I	4
Type II	22
Type III	3
Type IV	6
Others	2 (1.1%)
Delayed wound healing/wound infection	7 (3.8%)
Re-exploration for bleeding	2 (1.1%)
Stroke	2 (1.1%)
Deterioration of renal function	3 (1.6%)
Intervention of acute ischemia of limb	2 (1.1%)
Multiple organ failure (Liver, Kidney)	1 (0.5%)
Gastrointestinal complication	2 (1.1%)
Others	4 (2.2%)

Survival freedom from all-cause death, from aneurysm-related death and cardiovascular death at one year were $95.4 \pm 1.7\%$, $99.5 \pm 0.5\%$ and $96.6 \pm 1.5\%$ (**Fig. 2a–2c**), respectively. Two patients had a secondary procedure after dismissal. One was a coil embolization for expansion of internal iliac artery. The other was an extension of the iliac limb for a type I endoleak. Major morbidities after discharge included renal failure requiring dialysis, aortic valve replacement for severe aortic stenosis and surgery for pancreatic cancer. With respect to late results of endoleak observed at the end of procedure, type I and III endoleak in 7 out of 8 patients had disappeared at 6 months after EVAR. One patient with residual endoleak required the extension of iliac limb for treating type I endoleak. Two out of six patients who had a type IV endoleak had persisted at the most recent follow-up CT examination. About half of the patients who had a type II endoleak were still visualized on the CT examination so far and were currently under observation.

Pre- and post-operative PPI

PPI at both preoperative and postoperative conditions were available in only 129 out of 183 patients. Distributions of grade 0–4 were shown in **Fig. 1**. Five out of 129 patients showed postoperative PPI were downgraded

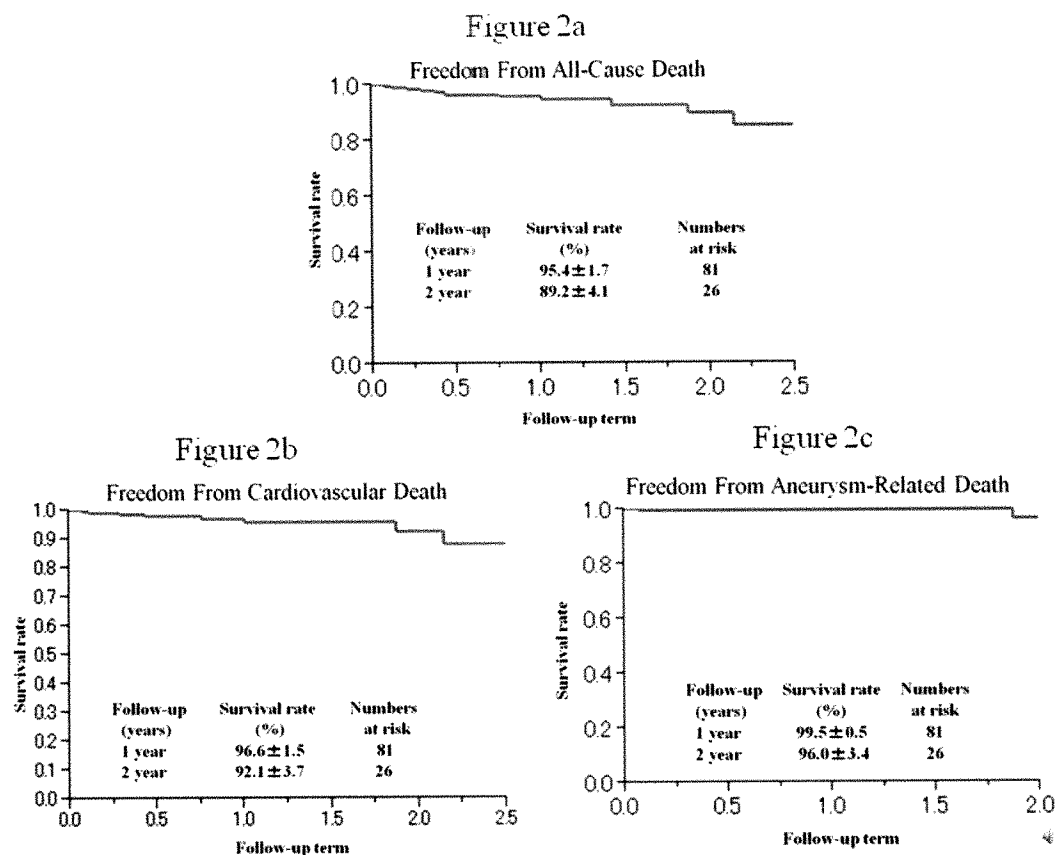


Fig. 2 Kaplan-Meier survival analysis freedom from-events.
a: Survival curve freedom from all-cause death.
b: Survival curve freedom from cardiovascular death.
c: Survival curve freedom from aneurysm-related death.

compared with preoperative PPI. All five patients had peri-procedural complications, including stroke and delayed wound healing. Physical performance was maintained in 59% of patients and was improved in 37%, while physical performance only in 4% of patients was downgraded (**Fig. 1**).

DISCUSSION

The present study showed the results of EVAR cases registered from eight NHO medical centers. It is clear that early mortality of 0.5% is good as a treatment modality, though 40 % of patients are more than or equal to 80 years old. Two prospective randomized trials published in 2004 and 2005 elegantly reported the early advantages of EVAR over open surgical repair in unruptured AAA cases,^{11–12)} which were updated with the data of long term follow-up.^{2–3)} Although most vascular surgeons and endovascular therapists in Japan accepted the results of two studies, they questioned why their mortalities of open

surgical results were relatively high. In contrast, the early mortality of open surgical repair surveyed by the Japanese Society for Vascular Surgery was about only 0.6%–0.9% in unruptured AAA.¹⁾ It is our question before the present study was conducted if the result of EVAR in Japan is low enough to be equivalent to the result of open surgical repair in Japan.

Most institutions of the NHO AAA study group were typical regional medical centers to start EVAR after it was authorized for health insurance reimbursement as well as federal approval as a treatment modality. Out of 8 NHO medical centers in the present study, three registered 30–50 cases, three did 10–30 cases and the other two did less than 10 cases. In general, the volume-outcome effect of the institution performing a large number of cases had better results compared with those performing a small number of cases and is also applied in the treatment of AAA.^{13–14)} Although they experienced a low to medium volume of EVAR cases, the overall results were excellent, which demonstrated that it is an extremely

safe procedure with a minimal learning curve. It also suggested that the introduction of the treatment modality into Japan has been very successful.¹⁵⁾ The Japanese Committee for Stentgraft Management (JACSM) was established to aim at the safe and proper practice standard for EVAR. It was reported recently that early mortality of EVAR in Japan was 0.4% in the first two years, analyzed by The JACSM.¹⁵⁾ The lower operative mortality in our study compared with the previous two prospective randomized trials in Europe could result from the difference of devices used when studies were conducted. Three devices currently available in Japan are very sophisticated, reliable and well-tested ones of the third-generation. In our study, treatments were performed more recently, from 2007–2010 compared with 1999–2003 in EVAR-1 and DREAM trials.^{11–12)} The most recent randomized trial from the Veterans Affairs (VA) Cooperative study in the United States was based on data between 2002 and 2007, which showed a 0.5% early mortality in the EVAR group.⁴⁾ The VA study excluded patients who had previous abdominal surgery or urgent repair. As a new generation of devices becomes available, which are modified, early results may further improve in the future.

With respect to preoperative risk evaluation in the present study, patients who had EVAR carried a variety of risks associated with cardiovascular disease, respiratory insufficiency, hostile abdomen and so on. As a result, the ASA physiological status before surgery showed that three fourths had at least mild systemic disease and 21% had severe systemic disease. In terms of the EVAR procedure and recovery from it, it was noted that the procedure time was short and the average volume of blood transfusion was a small amount. Duration of ventilator management and terms for starting oral intake and walking were very short as well, so that the hospital stay was less than 10 days on average. In addition, readmission within 30 days was required in only 5 cases (2.7%). Postoperative recovery appeared to be fast and smooth, though it was not compared with open surgical patients. With respect to the late results, mean duration of the follow-up term was only 1.0 years which is too short to elucidate a meaningful interpretation. No late re-intervention was reported so far except for two events: coil embolization in one patient and extension of leg for type I endoleak in another. It is, however, noted that the survival rate free from aneurysm-related death was 99.6% at one year. It is essential to collect longer follow-up data and to accumulate further case registration. It is also important to compare EVAR with open surgical repair. Prospective

randomized trial is required in Japan as well for demonstrating any evidence of relative advantage. At this moment in our study group, retrospective registration of open surgical repair is ongoing. The choice of treatment modality between two may not only depend upon surgical risk, but also upon other factors such as physical activity, quality of life, co-morbid conditions and cost-effectiveness in Japanese health insurance system. In the present study, PPI was used for estimating physical daily activity before and after surgery. Physical performance was maintained in 59% of patients and was improved in 37%. It is suggested that EVAR prevent deterioration of physical activity, while repairing AAA.

Limitation of the study

The present interim report has many limitations. It is obvious that the report is based on the data collected retrospectively. The report is only a descriptive observation without any intergroup comparison. Therefore the results are assessed in comparison with the previously published article outside Japan. The follow-up term was short. A longer follow-up and further accumulation of registered cases were mandatory.

CONCLUSION

Although a substantial portion of patients carry a variety of risks, good early outcomes were demonstrated in multicenter cooperative study of EVAR registration by eight NHO medical centers. It is suggested from the present data that EVAR is an acceptable alternative treatment modality to maintain physical performance well while repairing AAA.

ACKNOWLEDGMENT

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REFERENCES

- 1) Annual survey of vascular surgical cases by The Japanese Society for Vascular Surgery. <http://jsvs.jp/enquete6.php/result/index.html>
- 2) United Kingdom EVAR Trial Investigators, Greenhalgh RM, Brown LC, Powell JT, Thompson SG, Epstein D, et al. Endovascular versus open repair of abdominal aortic aneurysm. *N Engl J Med* 2010; **362**: 1863-71.
- 3) De Bruin JL, Baas AF, Buth J, et al. Long-term out-

- come of open or endovascular repair of abdominal aortic aneurysm. *N Engl J Med* 2010; **362**: 1881-9.
- 4) Lederle FA, Freischlag JA, Kyriakides TC, et al. Outcomes following endovascular vs open repair of abdominal aortic aneurysm: a randomized trial. *JAMA* 2009; **302**: 1535-42.
- 5) Lovegrove RE, Javid M, Magee TR, et al. A meta-analysis of 21,178 patients undergoing open or endovascular repair of abdominal aortic aneurysm. *Br J Surg* 2008; **95**: 677-84.
- 6) Grootenboer N, van Sambeek MR, Arends LR, et al. Systematic review and meta-analysis of sex differences in outcome after intervention for abdominal aortic aneurysm. *Br J Surg* 2010; **97**: 1169-79.
- 7) the Ministry of Education, Culture, Sports, Science and Technology, and the Ministry of Health, Labor and Welfare: Ethical guidelines for epidemiological research 17 June 2002.
- 8) Patterson BO, Holt PJ, Hinchliffe R, et al. Predicting risk in elective abdominal aortic aneurysm repair: a systematic review of current evidence. *Eur J Vasc Endovasc Surg* 2008; **36**: 637-45.
- 9) Owens WD, Felts JA, Spitznagel EL Jr. ASA physical status classifications: a study of consistency of ratings. *Anesthesiology* 1978; **49**: 239-43.
- 10) Oken MM, Creech RH, Tormey DC, et al. Toxicity and response criteria of the Eastern Cooperative Oncology Group. *Am J Clin Oncol* 1982; **5**: 649-55.
- 11) EVAR trial participants. Endovascular aneurysm repair versus open repair in patients with abdominal aortic aneurysm (EVAR trial 1): randomised controlled trial. *Lancet* 2005; **365**: 2179-86.
- 12) Blankensteijn JD, de Jong SE, Prinssen M, et al. Dutch Randomized Endovascular Aneurysm Management (DREAM) Trial Group. Two-year outcomes after conventional or endovascular repair of abdominal aortic aneurysms. *N Engl J Med* 2005; **352**: 2398-405.
- 13) Holt PJ, Poloniecki JD, Gerrard D, et al. Meta-analysis and systematic review of the relationship between volume and outcome in abdominal aortic aneurysm surgery. *Br J Surg* 2007; **94**: 395-403.
- 14) Holt PJ, Poloniecki JD, Khalid U, et al. Effect of endovascular aneurysm repair on the volume-outcome relationship in aneurysm repair. *Circ Cardiovasc Qual Outcomes* 2009; **2**: 624-32.
- 15) Obitsu Y, Ishimaru S, Shigematsu H. The education system to master endovascular aortic repair in Japan - the Japanese Committee for Stentgraft Management. *Eur J Vasc Endovasc Surg* 2010; **39**: S5-9.

APPENDIX

This is a research by National Hospital Organization Network Study Group in Japan for Abdominal Aortic Aneurysm.

Participants

Nobuhiro Handa, MD, Takeshi Nishina, MD, Yoichirou Ueno, MD, *Department of Cardiovascular Surgery, Nagara Medical Center, Nagara, Gifu, Gifu, Japan*
Toshihiro Onohara, MD, Keiichi Akaiwa, MD, Tadashi Furuyama, MD, MD, *Department of Vascular Surgery, Kyusyu Medical Center, Fukuoka, Fukuoka, Japan*
Jyunichi Kei, MD, Minoru Okamoto, MD, *Department of Cardiovascular Surgery, Kumamoto Medical Center, Kumamoto, Kumamoto, Japan*
Tsuyoshi Yamamoto, MD, *Department of Cardiovascular Surgery, Iwakuni Medical Center, Iwakuni, Yamaguchi, Japan*
Yasushi Shimoe, MD, *Department of Cardiovascular Surgery, Zentsuji Medical Center, Zentsuji, Kagawa, Japan*
Mikizou Nakai, MD, Masahiro Okada, MD, *Department of Cardiovascular Surgery, Okayama Medical Center, Okayama, Okayama, Japan*
Toshiki Takahashi, MD, Hitoshi Suhara, MD, *Department of Cardiovascular Surgery, Osaka Medical Center, Osaka, Osaka, Japan*
Fuminari Kasashima, MD, Masamitsu Endo, *Department of Cardiovascular Surgery, Kanazawa Medical Center, Kanazawa, Ishikawa, Japan*

➤ **Original Article** ✎

Outcome of the External Carotid Artery Following Carotid Endarterectomy with Added External Carotid Artery Eversion Endarterectomy

Mamoun Al-Basheer, MBBS (Lond), JBS FRCSI, FRCSEd, JBVS, FICA, D Ferrar, MD, FRACS, D Nelson, MHS, DMU (Vasc), and Theodor Vasudevan, MD, FRACS

Objective: To study the results of eversion endarterectomy of the external carotid artery (ECA) performed as part of standard CEA at a tertiary referral center using duplex ultrasonography.

Materials and Methods: Sixty patients (18 women and 42 men) who underwent 65 carotid endarterectomies at Waikato Hospital between January 2006 and July 2007 for significant internal carotid artery (ICA) disease were studied. The procedure also included eversion endarterectomy of the ECA with sharp transection at eversion end point. Preoperative and postoperative duplex scans were performed for all patients using Acuson (USA) ultrasound machine and by one sonographer. Postoperative follow-up scans at periods between 6 weeks and 18 months were reviewed and analyzed with Ascer et al. Doppler ultrasound-scan peak systolic velocity (PSV) criteria.

Results: Preoperative scans revealed significant bifurcation disease involving both ICA and ECA in all patients. The first post operative scan, done six weeks post-operatively, revealed one incomplete ECA endarterectomy, resulting in moderate (50%–74%) stenosis, while the rest had no evidence of residual ECA disease at the site of ECA endarterectomy. Over the post-operative period, sixteen (24.6%) ECA lesions and no occlusions were reported. The degree of ECA stenosis ranged from moderate to severe with PSVs ranging from 120 to 461 cm per second. All ECA lesions were ostial. Only 3 (18.7%) lesions were detected in the first nine months post operatively. Fifteen lesions were smooth and regular on duplex, while one had features of irregular residual stenosis. Eight (50%) were isolated ECA lesions, while the rest was associated with either ICA restenosis or occlusion.

Conclusion: ECA disease progression detected by Duplex ultrasound following eversion endarterectomy, as a part of CEA, commonly happens after 9 months and results in recurrent ECA stenosis, in most cases. Timing and features of the lesions suggest an intimal reaction as the aetiology in most cases. Eversion endarterectomy of the ECA does not predispose to ECA occlusion.

Key words: external, carotid, eversion, endarterectomy, duplex

Department of vascular surgery, Waikato Hospital, Hamilton, New Zealand

Received: February 26, 2011; Accepted: May 17, 2011
Corresponding author: Mamoun Al-Basheer, MBBS(Lond), JBS FRCSI, FRCSEd, JBVS, FICA. Department of Vascular Surgery, Waikato Hospital, Hamilton, New Zealand
Tel: 009626795637936, Fax: 0096265851876
E-mail: drbasheer30@yahoo.com

INTRODUCTION

The role of the external carotid artery as a major contributor to collateral blood flow to the brain once the internal carotid artery (ICA) is occluded or stenosed is well established.^{1,2)}

The progression of the external carotid artery (ECA) disease following CEA and its neurological outcome has been the subject of some debate with some suggesting that ECA endarterectomy predisposes to ECA occlusion.^{2,3)}

Table 1 Results of pre operative scans

ECA Disease		Associated ICA Disease	
Degree of Stenosis	Number of Vessels	Degree of Stenosis	Number of Vessels
50%–74%	6	50%–70%	1
		>70%	5
>74%	59	50%–70%	1
		>70%	58

This is particularly relevant with the advent of ICA stenting where the role of ECA is completely overlooked.

In this retrospective study, we aimed to follow the progression of ECA disease following CEA with added ECA eversion endarterectomy by duplex ultrasound. Timing of appearance and ultrasonographic features of ECA lesions are evaluated as an indication of possible etiology.

MATERIALS AND METHODS

The study group consisted of 60 patients (18 women and 42 men) who underwent 65 CEAs at Waikato Hospital between January 2006 and July 2007. The mean age was 67 years (range 59 to 78). All patients included in the study had significant bifurcation disease with stenosis in both internal and external carotids.

All patients had standard CEA for high grade ICA stenosis (symptomatic in 68% and asymptomatic in the rest).

The most common risk factor was smoking (66%). Other risk factors included diabetes mellitus (24%), hypertension (63 %), and coronary artery disease (64 %).

The CEA technique involved transmedial endarterectomy of the common and internal carotids ending with eversion of the proximal ECA as far as possible without opening the artery. To avoid intimal flaps, we released the occluding ECA clamp and then performed a sharp transection of the endpoint. Should the plaque break off with eversion, no further action was taken. All patients had patch repair of the carotid endarterectomy site.

Preoperative and postoperative duplex scans were performed for all patients using the same machine and by the same technologist. Postoperative follow-up scans at periods between 6 weeks and 18 months were reviewed and analyzed with Ascer et al. Doppler ultrasound-scan PSV criteria: <150 cm/s = 50% stenosis, 150 cm/s to 250 cm/s = 50% to 74% stenosis, and 250 cm/s = 75% stenosis.¹⁾

Data analysis is presented as the mean and a range or a

nominal value with a percentage.

RESULTS

No deaths or significant neurologic deficits were reported during the study period.

Pre operative scans revealed the distribution of disease detailed in **Table 1**. No vessel occlusions were detected preoperatively.

The first post operative scan done six weeks post-operatively reported widely patent CEA site in all. One patient had incomplete ECA endarterectomy resulting in moderate (50%–74%) stenosis while the rest had no evidence of residual ECA disease at the site of endarterectomy.

Subsequent follow-up scans revealed sixteen (24.6%) ECA lesions in 16 patients (12 men and 4 women).

The degree of stenosis included 5 (31.2%) external carotids with <50% stenosis and a mean PSV of 134 cm per second (range 120 to 148), and 7 (43.84%) with moderate stenosis (50% to 74%) and a mean PSV of 176 cm per second (range 154 to 241). Severe stenosis (>74%) was present in 4 (25%) external carotids with a mean PSV of 312 cm per second (range 262 to 461). The distribution into different degrees of stenosis is shown in **Fig. 1**.

All ECA lesions were ostial. Only 3 (18.7%) lesions were detected in the first 9 months post operatively. Eight (50%) were isolated ECA lesions: 7 were associated with mild (<50%) ICA restenosis and 1, with moderate (50% to 70 %) ICA restenosis.

DISCUSSION

The importance of the ECA has been well documented as a source of collateral flow to the brain. Fearn et al. demonstrate that the ipsilateral ECA contributes at least 10% to 15% of middle cerebral blood flow in patients with severe ICA stenosis. The most important of these extracranial-to-intracranial collaterals is through the

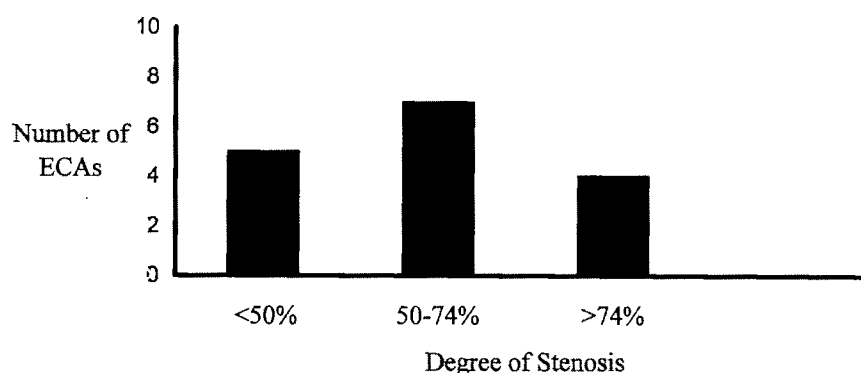


Fig. 1 The distribution into different degrees of stenosis.

ECA, collateralizing primarily through the periorbital plexus.^{2,3)}

Technical perfection is of paramount importance in performing carotid artery surgery, perhaps more than any other vascular reconstructive procedure, because of the potential danger of devastating perioperative stroke.⁴⁾

The importance of ECA patency was further emphasized by a study by Paty et al., where they found that treatment of external carotid disease, when flow cannot be restored to the ICA, also increases stroke-free survival, as compared with natural history data of up to 20% per year risk of recurrent stroke after nonoperative management of the ICA occlusion.⁵⁾

ECA occlusion or intimal flap after CEA presents as a potential source for either chronic embolization or a site for extended thrombosis and embolization in the acute situation.^{5,6)}

Amongst some technical variables in performing CEA, the method of removing plaque at the ECA has not been subject to a uniform approach, with a simple transection of the plaque at the orifice, blind endarterectomy into the lumen of the artery, or eversion endarterectomy; all being potential options for completing the endarterectomy in this area.^{1,6)}

The ECA is not usually treated in the same meticulous manner as the ICA during endarterectomy of the carotid bifurcation, where it is mostly endarterectomized in a blinded fashion. Undoubtedly, the rationale for this is to minimize the operative time, and specifically, the duration of carotid occlusion.²⁾

While the results of endarterectomy of ICA and common carotid artery have been excellent, scattered reports of less than acceptable short- and long-term results have

been noted when these approaches are taken with the ECA. A partial explanation for this may be differences in the flow characteristics of the ECA, vis a vis the ICA and CCA, as well as the techniques utilized in handling the endpoint in the traditional approach to the ECA.⁷⁾

Our operative technique of performing the endarterectomy involves the use of regional anesthesia or general anesthesia with an ICA stump pressure measurement, selective shunting, and a standardized procedure (see methods) that includes a sharp ECA plaque transection.

Carotid duplex scans were performed by the same vascular technologist using the same machine at Waikato Hospital vascular laboratory. The interpretation of ECA disease was obtained from cross-sectional and longitudinal B-mode ultrasound imaging, as well as from Doppler PSV measurements, based on the measurements of Ascer et al., who contributed a set of duplex-scan PSV criteria for ECA stenosis, on the basis of the magnetic resonance angiography of 60 arteries: <150 cm/s = 50% stenosis, 150 cm/s to 250 cm/s = 50% to 74% stenosis, and ≥250 cm/s = ≥75% stenosis.^{1,6)}

Ascer et al. reported a 100% ECA patency rate and an 18% incidence rate of 50% stenosis and a 10% incidence rate of 75% residual or operatively produced ECA stenosis in the first month after CEA with simple transection of the plaque at the ECA orifice.¹⁾

Our results were comparable with those of only one patient, having what seemed to be residual plaque from surgery detected by the first post operative scan, done within 6 weeks after surgery.

When endarterectomy relieves bifurcation stenosis, common carotid artery blood flow is redistributed

preferentially to the ICA at the expense of ECA flow, consistent with a change in the relative resistances of the two vessels resulting from operative reconstruction.^{8,9}

The timing of recurrence of most stenoses during a 9- to 18-month period, in addition to the ostial location, would suggest intimal hyperplasia and recurrent disease as primary etiologies.

Further research in the area with linkage to clinical outcome is needed.

CONCLUSION

Duplex ultrasonography shows that the ECA stays patent following CEA with eversion endarterectomy of the ECA and sharp transection of endarterectomy endpoint but is prone to recurrent stenosis. The timing of the stenosis indicates intimal hyperplasia and disease progression as possible aetiologies.

Our data further supports previous work in this field, which suggests the stability of the ECA plaque and the low likelihood of its progressing to an occlusion.

REFERENCES

- 1) Archie JP Jr. The outcome of the external carotid endarterectomy during routine carotid endarterectomy. *J Vasc Surg* 1998; **28**: 585-90.
- 2) Byrne JL, Zaman SN. External carotid endarterectomy under direct vision. *Am J Surg* 1989; **157**: 243-4.
- 3) Fearn SJ, Picton AJ, Mortimer AJ, et al. The contribution of the external carotid artery to cerebral perfusion in carotid disease. *J Vasc Surg* 2000; **31**: 989-93.
- 4) Papanicolaou G, Toms C, Yellin AE, et al. Relationship between intraoperative color-flow duplex findings and early restenosis after carotid endarterectomy: a preliminary report. *J Vasc Surg* 1996; **24**: 588-96.
- 5) Paty PS, Adeniyi JA, Mehta M, et al. Surgical treatment of internal carotid artery occlusion. *J Vasc Surg* 2003; **37**: 785-8.
- 6) Ascer E, Gennaro M, Pollina RM, et al. The natural history of the external carotid artery after carotid endarterectomy: implications for management. *J Vasc Surg* 1996; **23**: 582-5.
- 7) Ascher E, Hingorani A, Markevich N, et al. Carotid surgery without external carotid endarterectomy: a 6-year clinical experience with 1027 cases. *Eur J Vasc Endovasc Surg* 2003; **25**: 458-61.
- 8) Brothers TE. Initial experience with eversion carotid endarterectomy: absence of a learning curve for the first 100 patients. *J Vasc Surg* 2005; **42**: 429-34.
- 9) Gordon IL, Stemmer EA, Wilson SE. Redistribution of blood flow after carotid endarterectomy. *J Vasc Surg* 1995; **22**: 349-58.

➤ Original Article ◀

Three-dimensional CT Venography: A Diagnostic Modality for the Preoperative Assessment of Patients with Varicose Veins

Katsutoshi Sato, MD,¹ Kazumasa Orihashi, MD,¹ Shinya Takahashi, MD,¹ Taiichi Takasaki, MD,¹
Tatsuya Kurosaki, MD,¹ Katsuhiko Imai, MD,¹ Minoru Ishifuro, PhD,² and Taijiro Sueda, MD¹

Objective: We preoperatively assessed varicose veins by means of computed tomography (CT) with contrast injection in the veins of the lower extremity (CT venography). This paper reports the procedures, results and implications of CT venography from the surgical aspect.

Methods: A total of 48 legs in 39 patients were examined. Contrast medium was diluted ten-fold and injected into the lower extremity veins, often using a dual route of injection. The images were reconstructed with the volume-rendering method.

Results: CT venography clearly visualized the veins with a small amount of contrast medium and facilitated the identification of anatomy that was not suitable for passing the stripper. In addition, CT venography helped identify unusual types of varicose veins or uncommon sites of inflow of small saphenous veins. Such information was helpful for avoiding unexpected vascular injury or for minimizing skin incision. Dual-route injection was beneficial to minimize the blind zones. Doppler ultrasound could be more focused on hemodynamic assessment and determination of incision sites.

Conclusions: CT Venography is feasible in all cases of varicose veins. When performed in conjunction with ultrasonography, it appears to facilitate the safe and efficient treatment of various types of varicose veins.

Key words: computed tomography, venography, varicose vein

INTRODUCTION

A number of treatments for varicose veins have been introduced including stripping, subfascial endoscopic perforator surgery (SEPS)¹⁾ and endovenous laser ablation (EVLA).²⁾ In these procedures, evaluation of the venous system in the entire lower extremity is essential

for safe and effective treatment. Preoperative assessment in detail is especially important in the selective stripping operation, which is designed to minimize complications.³⁾ Several modalities have been used for this purpose including venography,⁴⁾ Doppler ultrasound,⁵⁾ computed tomography (CT),^{6–8)} and magnetic resonance imaging (MRI)⁹⁾; however, all of these methods have limitations.

Doppler ultrasound is noninvasive and provides morphological and hemodynamic information, but it takes time for scanning the entire leg, and the accuracy and quality of assessment depends on the skill of the examiner. Although venography gives an image of the entire length of the lower extremity veins, the image is often inadequate despite the use of a large volume of contrast medium. While these modalities provide only two-dimensional information, multi-detector contrast CT has enabled three-dimensional imaging using the volume-rendering method. However, we have often experienced images of the veins taken in the late phase that were not

¹Department of Surgery, Division of Clinical Medical Sciences, Graduate School of Biomedical Sciences, Hiroshima University, Hiroshima, Hiroshima, Japan

²Division of Radiology, Hiroshima University, Hiroshima, Hiroshima, Japan

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Corresponding author: Katsutoshi Sato, MD, Department of Surgery, Division of Clinical Medical Sciences, Graduate School of Biomedical Sciences, Hiroshima University, Kasumi 1-2-3, Minami-ku, Hiroshima, Hiroshima 734-8551, Japan
Tel: +82-257-5219, Fax: +81-82-257-5216

E-mail: satoktts@hiroshima-u.ac.jp

clear compared with the images of arteries in the early phase, and imaging requires a large volume of contrast media of up to 2 ml/kg (maximum 150 ml).⁶⁻⁸⁾

Therefore, we adopted "CT venography" that is, three-dimensional CT combined with venography using dilute contrast medium injected into the veins of the lower extremity, to obtain clear 3D images in the early phase of injection with the volume-rendering method. A similar method was reported in 2003 by Uhl et al.¹⁰⁾ in two illustrative cases. To date, however, this method has not gained widespread acceptance. Thus, we have further refined this method for preoperative assessment of varicose veins. This paper describes the details of CT venography including the technical aspects of this method and the selection of a surgical strategy based on the information provided by this method.

METHODS

Subjects

We examined 39 consecutive patients with varicose veins who underwent surgical treatment in our hospital between February 2006 and March 2008. The patients included 16 males and 23 females with ages ranging from 29 to 78 years old (mean age, 63.3 years old). Nine patients had bilateral varicose veins, and a total of 48 legs were examined. Patients who were allergic to iodine or had deep vein thrombosis were excluded. The varicose veins were of the great saphenous type, small saphenous type, or non-saphenous type in 34, 11, and 3 legs, respectively. The grading of varicose veins according to the clinical classification¹¹⁾ was C2, C3, C4, C5, and C6 in 11, 6, 22, 6, and 3 legs, respectively. The indication for surgery was determined following the physical examination. The surgical strategy and precise location of the incision was determined based on the CT findings and ultrasonography. This study was approved by the Ethical Committee at our institute, and informed consent was obtained from every patient.

Injection route and posture

Contrast medium was injected through a 22-gauge angiocatheter. The injection route for the great saphenous vein was at the inside of the dorsum of the foot, and that for the small saphenous vein was around the external malleolus. When the vein around the external malleolus was difficult to cannulate due to hard skin or a non-dilated, small saphenous vein, the route was placed distal to the varicose vein of the calf. In such instances, the great

saphenous vein route was also used to minimize the blind zones. In those cases with a non-saphenous type of varicose vein or history of previous surgery, similar dual-injection routes were used to minimize regions of poor visualization or the need for additional examination. With the dual-injection route, contrast medium was injected through a bifurcated delivery system with one injector.

The patients were placed in a semi-Fowler position at about 45 degrees using a triangle backrest so that the contrast medium stayed in the lower extremity veins. In addition, 5-cm thick blocks were placed under the heel and the hip to avoid compression of the veins on the dorsal side of the lower extremity.

CT study

Contrast medium for injection was prepared by diluting 15 ml of nonionic contrast medium (300 mgI/ml: IopamironTM, Fuji Pharmaceutical Co., Tokyo, Japan) with 135 ml of normal saline to avoid halation of the CT images. We determined that the optimal density for obtaining sharp 3D images of the saphenous, perforator and deep veins in the entire lower extremity with the volume-rendering method was approximately 500 HU (Hounsfield units).¹²⁾ We conducted a preliminary study by imaging various dilutions of contrast medium in a test tube, and concluded that a ten-fold dilution was suitable for CT venography.

CT studies were performed using a 16-multi-detector-row CT (Light Speed Ultra 16; GE Medical System, Milwaukee, WI, USA). Contrast medium was injected into the vein with an automated injector (DUAL SHOT A-250; Nemoto Kyorindo Co., Ltd. Osaka Japan) at a rate of 3.5 ml/s under pressure monitoring (43 seconds for injection of 150 ml) while the patient was breathing normally. The optimal time delay before scanning was examined in the first two cases. The veins were adequately visualized when scanning was started 5 seconds before the end of injection, but contrast medium was partially washed away when scanning was started 30 seconds after the injection was finished. Thus, we adopted the former protocol in the remaining cases. The scanning parameters were as follows: table speed, 27.5 mm per rotation; beam pitch, 1.375; tube current, 300 mA; rotation time, 0.7 second; and voltage, 120 kVp. Imaging was completed with a single scan from the foot to the anterior superior iliac spine without tourniquets or leg compression, which is commonly used in venography. The time required for imaging including injection and scanning was approximately one minute. CT Dose Index (CTDI) volume was 8.15 mGy.

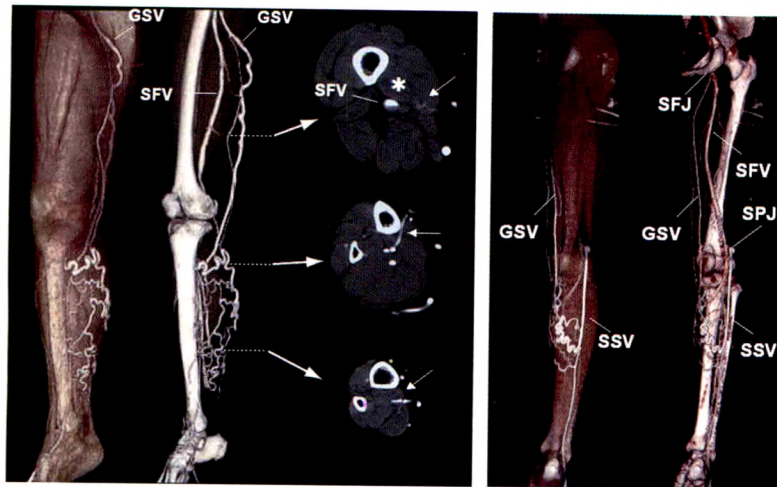


Fig. 1 Venography CT images: superficial 3D view (left) and deep 3D view (right).

A: great saphenous vein type. * Axial views of the thigh are shown. In the superficial femoral vein, a partial filling defect mimicking deep vein thrombosis was noted. **B:** small saphenous vein type. Saphenous vein, deep veins and perforators in the entire extremity are clearly visualized.

SFV: superficial femoral vein; GSV: great saphenous vein; SFJ: saphenofemoral junction; PV: popliteal vein; SSV: small saphenous vein; SPJ: saphenopopliteal junction

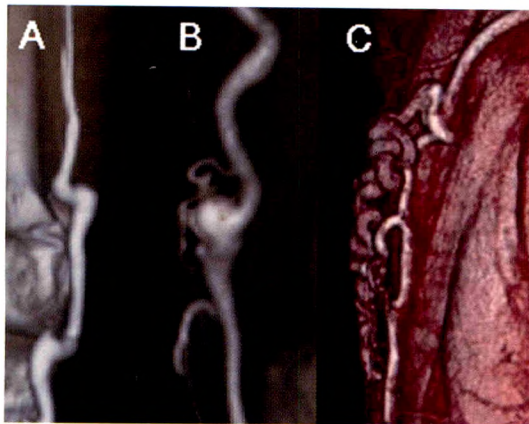


Fig. 2 Unusual course of the saphenous vein visualized with CT venography.

A: angulated course of the vein. **B:** venous aneurysm. **C:** large branch connected to the varicose vein. These can lead to unexpected vein injury during the stripping procedure.

Three-dimensional images were reconstructed with the volume-rendering method using commercially available software (Virtual Place Raijin, AZE, Ltd. Tokyo Japan) by radiological technicians. It took a few seconds for processing our set template in the workstation. Three patterns of images were provided for preoperative assessment: 1) axial view; 2) 3D-images of superficial veins and muscles (superficial 3D view); and 3) 3D-images with superficial and deep veins, perforators and bones (deep 3D view). When needed, coronal and/or sagittal images were obtained.

RESULTS

Imaging was completed in all cases. According to the above protocol, the veins were clearly visualized without arterial images in every case. The average density of the

venous lumen in the initial 15 cases was 745 ± 103 HU in the saphenous trunk adjacent to the injection route and 437 ± 74 HU in the great saphenous vein near the saphenofemoral junction. Density in the deep vein was nearly the same as that at the corresponding level in the superficial vein.

The CT venographic images of the great and small saphenous veins are shown in **Fig. 1A** and **1B**. The saphenous veins were clearly visualized in the superficial 3D view; and perforators, in the deep 3D view. Perforators (Dodd, Boyd, or Cockett veins) are depicted in the axial view (arrows). There was no interference or masking by arterial images. The CT venographic views distinctly identified the position of the perforator behind the tangled varicose veins and facilitated Doppler assessment and selection of the incision site. As noted in these views, however, the distal portion of the great saphenous vein was poorly visualized when contrast medium was injected into the small saphenous vein only.

Figure 2 shows three types of great saphenous varicose veins that can be troublesome during the advancement of a stripper. CT venography revealed an angulated course of the vein (**Fig. 2A**), venous aneurysm along the vein (**Fig. 2B**), or the presence of a large branch connected to the varicose vein (**Fig. 2C**). In the former two types, the vein can be easily perforated at the angulation or venous aneurysm as the stripper is blindly advanced. In the presence of a large branch, the stripper can enter the branch. In those cases, the troublesome portion was accurately located with ultrasonography, guided by 3D-CT images, and an additional small incision was added for dividing the saphenous vein or for ligating the branch and removing the varicose vein.

Uncommon types of varicose veins are shown in **Fig. 3**.

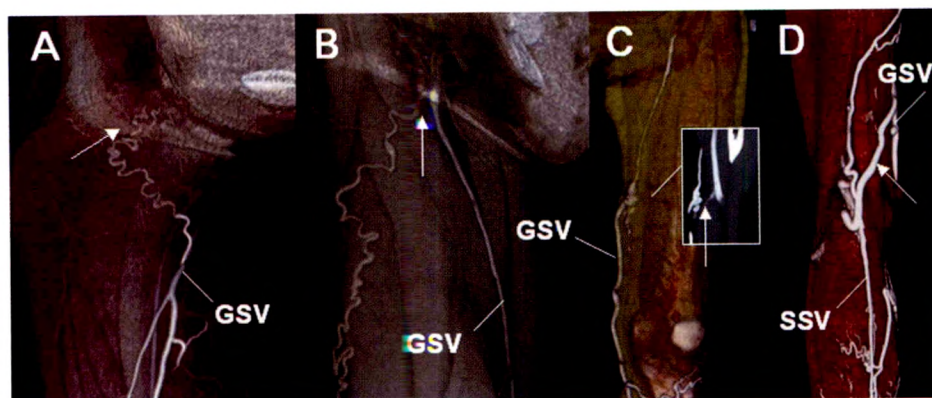


Fig. 3 Uncommon types of varicose veins.

A: Vulval varicose vein (arrow) with normal saphenofemoral junction and slightly dilated saphenous trunk. **B:** Branched saphenous vein (arrow) causing regurgitation at the saphenofemoral junction, but without regurgitation in the saphenous trunk. **C:** Distal portion of great saphenous varicose vein due to incompetent perforator (arrow). **D:** Giacomini vein (arrow) with regurgitation of saphenopopliteal junction and dilated great saphenous vein. SFV: superficial femoral vein; GSV: great saphenous vein; SSV: small saphenous vein

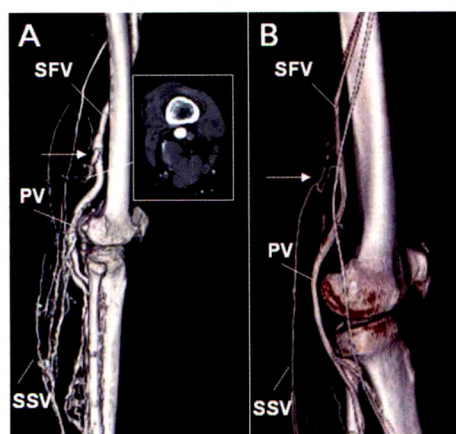


Fig. 4 Small saphenous vein connecting to the femoral vein. There is no connection to the popliteal vein (white arrow). **A:** Venous aneurysm of small saphenous vein with a large thrombus (black arrow). **B:** Division into several small veins.

SFV: superficial femoral vein; PV: popliteal vein; SSV: small saphenous vein

Figure 3A shows a vulvar-type of varicose vein with an intact saphenofemoral junction. The upstream of the saphenous vein was dilated. With the aid of CT venography, the most downstream (arrow) was located for ligation, and connecting perforators were examined. In another case, regurgitation was present in one of the tributaries (arrow) of the saphenofemoral junction but not in the saphenous vein (**Fig. 3B**). Ligation of this tributary and the saphenofemoral junction were done. To visualize these images, we had to cannulate the varicose vein in the pos-

terior-to-lateral aspect of the lower extremity. **Figure 3C** shows a varicose vein with an intact saphenofemoral junction, which originated in the middle of the great saphenous vein due to an incompetent perforator (arrow). The incompetent perforator was ligated, and the distal portion of the great saphenous vein was selectively stripped. **Figure 3D** demonstrates a varicose vein due to the Giacomini vein (arrow). The small saphenous vein was ligated at the saphenopopliteal junction, and the Giacomini vein and great saphenous vein were selectively stripped. Although great-saphenous types of varicose veins were suspected in the cases shown in **Fig. 3**, CT venography revealed that they were uncommon types. Although these anatomical structures may be detected with Doppler ultrasound as well, CTV images were more comprehensive because of clear 3D images.

Although the small saphenous vein usually converges with the popliteal vein at the level of the knee joint, it flowed into the femoral vein in 4 of 11 cases with a small-saphenous type of varicose vein. Venous aneurysms were present at the junctions in 3 of these 4 cases, and they were associated with thrombus formation in 2 cases (**Fig. 4A**). In another case, the small saphenous vein divided into several small veins, which flowed into the femoral vein (**Fig. 4B**).

In every case, the CT venographic findings were confirmed by subsequent Doppler assessment and operative findings and the CT assessment proved to be correct, although statistical analysis was not applied. All cases were treated with selective stripping under tumescent

local anesthesia, and the distal part of the varicose veins in the lower extremity were not ligated or resected, and sclerotherapy was not performed. The residual varicose veins withdrew in several months, and no case required re-operation or additional sclerotherapy.

In the femoral-to-iliac vein, a partial filling defect mimicking deep vein thrombosis was noted in every case (**Fig. 1**, asterisk). Ultrasonography showed that there was no deep vein thrombus, and we concluded that this was an artifact in CT venography.

We experienced one complication in this series. Contrast medium leaked out of the vein during injection but did not lead to significant sequelae, because a dual-injection route was used and the contrast medium probably entered the venous system through the alternate route, reducing the amount of extravasation.

DISCUSSION

This study shows that CT venography, with topical injection of contrast medium, clearly visualizes the saphenous veins, perforators, and connecting deep veins, with one-tenth the volume of contrast medium.

CT venography with systemic vein injection of contrast medium has been reported by several groups.⁶⁻⁸⁾ By using over 100 ml of contrast medium, Lee et al. found that the density was approximately 150 HU in the veins of the lower extremity.⁷⁾ Despite a low enhancement level, they successfully differentiated the veins from surrounding tissues such as muscle or adipose tissue. This level is sufficient for obtaining the 3D images of superficial veins, which corresponds to our "superficial 3D view". However, it can be insufficient for visualizing the perforators and deep veins together with the varicose veins as shown in the "deep 3D view" in our study. Although a larger amount of contrast medium would improve visualization of the veins, it would also enhance the arterial images and make an accurate diagnosis difficult as well as increase the risk of renal damage.

Although our method necessitates uncommon injection routes, sufficient enhancement of the veins (around 500 HU) was obtained in every case with approximately one-tenth of the amount of contrast medium and without any arterial images. The risk of renal toxicity, as well as the cost, is reduced with less contrast medium.

This study demonstrated a number of clinical advantages of topical CT venography, in addition to those of systemic CT venography, including visualization of an angulated course of the vein or venous aneurysm (**Fig. 2**),

unusual types of varicose veins (**Fig. 3**), or uncommon sites of inflow into the deep veins (**Fig. 4**). Such information is helpful for minimizing unintended injury of the veins during stripping procedures or for avoiding an inappropriate incision or the need for an additional incision. Although elaborate assessment by ultrasonography may reveal such variances; clear, panoramic, three-dimensional CT venographic images facilitate the selection of an appropriate surgical strategy and are advantageous for minimizing interobserver variability. In our experience, the time required for ultrasonographic assessment was shortened by the information provided by CT venography. Since the anatomies of the varicose veins were clearly shown, the role of Duplex studies was mainly for locating the regurgitation to determine the incision site. Time for ultrasonographic assessment was reduced to approximately one-third when it is preceded by CT assessment.

Lee et al. indicated that the direct injection of diluted contrast medium into a varicose vein could possibly fail to opacify a portion of the vein.⁷⁾ We recognized this problem in the early cases, and introduced a dual-injection route when specific information was needed for adequate visualization of the veins. Injection into a varicose vein was found to be advantageous for adequate visualization of veins in cases with complicated varicose veins and/or recurrence after a previous surgery. However, we became aware of a pitfall in this procedure. When the catheter cannot be advanced to its full length, there may be possible leakage of contrast medium due to penetration of the vein wall or dropout of the catheter from the vein during injection, as was experienced in one case in our series.

We used 150 ml of diluted contrast medium based on our previous experience in venography. A total amount of 50 ml filled only the veins in the lower thigh, and the proximal portion of veins was visualized as the contrast media moved proximally. We felt that 150 ml of diluted contrast media was necessary to fill the entire venous lumen of the lower extremity. Since the vein is exclusively opacified with our method, it allows volumetric measurement of the venous lumen in the lower extremity. The measured volume of the venous lumen in the initial 15 cases was 187 ± 60 ml. This volume may be overestimated because the veins are scanned in a distal-to-proximal direction, while the contrast medium washed out during scanning. Thus, we concluded that 150 ml of diluted contrast medium is appropriate for CT venography.

Volume loading of 150 ml including normal saline in a short time could be a risk for those patients with cardiac

dysfunction, especially when the legs need to be examined bilaterally in elderly patients, although no such complication was encountered in this study. In contrast, the small amount of contrast medium (15 ml) needed for CT venography might not influence kidney function so much.

It is very apparent that CT venography does not provide hemodynamic information, and Doppler ultrasound is essential to confirm the reverse flow and to determine the incision site. However, information by CT venography was helpful for efficiently focusing the points of Doppler assessment. For example, an inflow from small saphenous veins to the femoral vein is not uncommon, as was experienced in 4 of 11 cases in this series (Fig. 4). Since the inflow may be as deep as 5 cm from the skin, locating the inflow site with ultrasonography in combination with CT images was advantageous for minimizing the skin incision and time required for the surgical procedure. The surgical procedures could be carried out under local anesthesia in every case. In patients with skin ulcers or chronic edema, it is often difficult to identify perforators with only Doppler ultrasound. Axial and 3D images from CT venography were helpful for identifying the perforators. These findings may be beneficial for SEPS. In this series, varicose veins were treated with stripping operations in all patients. Although EVLT is increasingly getting popularity in Japan, the CTV information may be helpful for understanding the unusual anatomy in the area scheduled for ablation.

A filling defect in the femoral-to-iliac vein is common in CT venography. This finding appears to be caused by the intermixing of venous return that contained no contrast medium. Although this finding can possibly be regarded as deep venous thrombosis, it is not important in clinical practice because ultrasonography readily rules out venous thrombosis.

Although ultrasonography has been mainly used to evaluate the varicose vein and provides sufficient information, it has limitations, as described above. CT venography is very easy, less invasive, and accurate method. Then, it might be indicated for all varicose veins, which is difficult to appreciate by ultrasonography.

CONCLUSIONS

CT venography allows clear visualization of the great and small saphenous veins, perforators and deep veins in the entire lower extremity without interference by arterial images. In addition, this method requires a small amount of contrast medium, which is advantageous for reducing cost and renal damage. Furthermore, it facilitates the

selection of effective and efficient strategies when it is used in conjunction with ultrasonography. CT venography may be an optional evaluation method for the treatment of varicose veins.

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REFERENCES

- 1) Kurdal AT, Cerrahoglu M, Iskesen I, et al. Subfascial endoscopic perforator surgery ameliorates the symptoms of chronic venous ulcer (C6) patients. *Int Angiol* 2010; **29**: 70-4.
- 2) Nadarajah ST, Demos D, Andrew IDM, et al. Endovenous laser ablation: dose standard above-knee great saphenous vein ablation provide optimum results in patients with both above- and below-knee reflux? A randomized controlled trial. *J Vasc Surg* 2008; **48**: 173-8.
- 3) Koyano K, Sakaguchi S. Selective stripping operation based on Doppler ultrasonic findings for primary varicose veins of the lower extremities. *Surgery* 1988; **103**: 615-9.
- 4) Kistner RL, Ferris, EB, Randhawa G, et al. A method of performing descending venography. *J Vasc Surg* 1986; **4**: 464-8.
- 5) Jutley RS, Cadle I, Cross KS. Preoperative assessment of primary varicose veins: a Duplex study of venous incompetence. *Eur J Vasc Endovasc Surg* 2001; **21**: 370-3.
- 6) Caggiati A, Ricci S, Laghi A, et al. Three-dimensional contrastless varicography by spiral computed tomography. *Eur J Vasc Endovasc Surg* 2001; **21**: 374-6.
- 7) Lee W, Chung JW, Yin YH, et al. Three-dimensional CT venography of varicose veins of the lower extremity: image quality and comparison with Doppler sonography. *AJR* 2008; **191**: 1186-91.
- 8) Min SK, Kim SY, Park JY, et al. Role of three-dimensional computed Tomography venography as a powerful navigator for varicose vein surgery. *J Vasc Surg* 2010; **51**: 893-9.
- 9) Koizumi J, Horie T, Muro E, et al. Magnetic resonance venography of the lower limb. *Int Angiol* 2007; **26**: 171-82.
- 10) Uhl JF, Verdeille S, Bouyer M. Three-dimensional spiral CT venography for the pre-operative assessment of varicose patients. *VASA* 2003; **32**: 91-4.
- 11) Beebe HG, Bergan JJ, Bergqvist D, et al. Classification and grading of chronic venous disease in the lower limbs. A consensus statement. *Int Angiol* 1995; **14**: 197-201.
- 12) Feil X, Du X, Yang Q, et al. 64-MDCT coronary angiography: phantom study of effects of vascular attenuation on detection of coronary stenosis. *AJR Am J Roentgenol* 2008; **191**: 43-9.

➤ Original Article ◀

Skin Perfusion Pressure Measurement to Assess Improvement in Peripheral Circulation after Arterial Reconstruction for Critical Limb Ischemia

Yoshiko Watanabe, MD, PhD,¹ Atsuko Onozuka,² Yukio Obitsu, MD, PhD,³ Hiroyoshi Komai, MD, PhD,¹
Nobusato Koizumi, MD, PhD,¹ Naozumi Saiki, MD,¹ and Hiroshi Shigematsu, MD, PhD⁴

Aim: To assess the utility of skin perfusion pressure (SPP) measurement in evaluating the outcome of vascular constructions for critical limb ischemia (CLI) patients.

Methods: We retrospectively studied 19 lower limbs in 18 patients who underwent arterial reconstruction for CLI from whom SPP measurements had been obtained pre- and postoperatively between 2008 and 2010. Six limbs whose ulcers had healed postoperatively were classified into group H, 7 limbs whose ulcers had not healed into group U, and 6 limbs without ulcers into group N. SPP values were compared among these groups.

Results: The preoperative SPP values in all groups were <30 mmHg, without significant differences among the groups. The SPP values in groups H and N significantly improved after operation, and those in group U were significantly lower than those in the other groups.

Conclusions: SPP measurement before and after arterial reconstruction is useful to assess improvement in tissue circulation and to predict the likelihood of wound healing. An SPP value ≥30 mmHg was considered necessary for wound healing, supporting the findings of the few reports in the literature on the usefulness of SPP for assessing vascular reconstruction effects on ulcer wound healing.

Key words: skin perfusion pressure, peripheral artery disease, arterial reconstruction, wound healing

INTRODUCTION

The number of patients with critical limb ischemia (CLI) due to peripheral artery disease (PAD) is increasing worldwide, and the need for arterial recon-

struction surgery has, therefore, become more frequent. When considering arterial reconstruction in such cases, there are several important clinical points which vascular surgeons attempt to clarify: the extent to which ischemia affects symptoms such as pain or ulcers; whether the indications for arterial reconstruction are certain or not; the extent to which the peripheral circulation of the patient had improved with the arterial reconstruction, and the safe perfusion level required for the optimal healing of ischemic ulcers.

For the assessment of these points, skin perfusion pressure (SPP) measurement is considered to be reliable and useful.^{1–5)} SPP measurement is a noninvasive method of estimating microcirculation of the limbs at a depth of 1.5 to 2.0 mm beneath the skin using a Doppler laser probe. The ankle-brachial pressure index (ABI) is internationally considered to be the optimum method to estimate peripheral circulation. However, patients with diabetes

¹Department of Vascular Surgery, Tokyo Medical University, Tokyo, Japan

²Vascular Laboratory, Department of Vascular Surgery, Tokyo Medical University, Tokyo, Japan

³Vascular Surgery Department, International University of Health and Welfare Mita Hospital, Tokyo, Japan

⁴Vascular Center, Sanno Medical Center, International University of Health and Welfare, Tokyo, Japan

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Corresponding author: Yoshiko Watanabe, MD, PhD. Department of Vascular Surgery, Tokyo Medical University, 6-7-1 Nishishinjuku, Shinjuku-ku, Tokyo 160-0023, Japan

Tel: +81-3-3342-6111, Fax: +81-3-3342-6193

E-mail: yosiyosi515@mac.com

mellitus or chronic kidney disease often have severely calcified peripheral arteries. A blood pressure cuff cannot sufficiently compress the ankle arteries, and, therefore, their ABI often shows false high values. Moreover, if the patient has additional lesions below the ankle, these cannot be evaluated using ABI. However, in such patients accurate evaluation of peripheral circulation is possible with SPP measurement and is unaffected by arterial calcification of arteries.^{6, 7)} SPP measurement can also be performed below the ankle and near the ulcer, can evaluate the insufficiency of smaller arteries,³⁾ and can predict the outcome of ulcers and wound healing.²⁾ Previous studies have concluded that ulcers and wounds in which the SPP decreases to <30 or 40 mm Hg do not heal.^{1, 2, 4–6)}

We started SPP measurements following the establishment of a vascular laboratory at our institution in August 2008. Although the number of examinations of SPP is still small in our institution at present, we deemed it useful to have an initial evaluation of its effectiveness by retrospectively assessing the changes in SPP values obtained between the pre- and postoperative periods^{8, 9)} and the relationship between the SPP values and ulcer healing, in order to assess the utility of SPP measurement in evaluating the outcome of arterial reconstructions in patients with CLI caused by arteriosclerosis obliterans (ASO).

MATERIALS AND METHODS

Between 2008 and 2010, we performed 84 vascular reconstructions in 74 patients with ASO at our institution. SPP was measured before and after arterial reconstruction in 19 lower limbs of 18 patients (15 men and 3 women, average age, 73.2 ± 6.7 years) with CLI (Fontaine stages 3 and 4). SPP was measured at the center of the distal portion of the plantar and/or dorsal area of the foot, pre- and postoperatively.

SPP was measured using the SensiLase PAD 3000 (Vasamed Inc., Eden Prairie, MN, USA) at room temperature with the patient in the supine position. We used a laser Doppler probe positioned underneath a 5.8-cm-wide blood pressure cuff (laser pressure transducer (LPT) cuff) wrapped around the patient's foot. The specific dates of SPP measurement pre- and postoperatively were not decided, but the usual date for postoperative examination was after the pain and swelling in the foot had subsided.

We divided the patients into 3 groups. Those whose ischemic ulcers had healed after arterial reconstruction were classified into group H. Those whose ischemic

ulcers had not healed were classified into group U. Those without ischemic ulcers at any time during the observation period were classified into group N.

All statistical analyses were performed with JMP statistical software (version 7.0.1; SAS Institute, Cary, NC, USA). Results are shown as means $\pm$ standard deviation (SD). Multiple comparisons of average values among the 3 groups were analyzed using the Tukey-Kramer honestly significant difference (HSD) test. *P* values less than 0.05 were considered to represent a statistically significant difference among the groups. Comparisons of average SPP values pre- and postoperatively were analyzed using the Wilcoxon signed-rank test. The Pearson chi-square test was used to analyze the ratio of underlying atherosclerotic risk factors.

RESULTS

Among a total of 19 lower limbs of 18 evaluable patients, 6 limbs were classified into group H (measurements obtained at 13 points), 7 into group N (measurements obtained at 16 points), and 6 into group U (measurements obtained at 16 points). One limb in group U had a deep ulcer with exposed toe bones and methicillin-resistant *Staphylococcus aureus* (MRSA) infection. Another limb in group U had a large ulcer on the entire heel with MRSA infection. Other ulcers in groups H and U were located on the skin surface of the toe of each limb. The demographic characteristics and atherosclerotic risk factors of the patients are shown in **Table 1**. The number of patients did not differ significantly among the 3 groups in terms of any diseases; however, there were more patients with cerebral vascular disease in group N than in the other groups. Moreover, although not significantly different, the number of patients receiving hemodialysis was the largest in group U, followed by group N, and then finally group H, reflecting the prevalence rate of renal disorder in these groups.

The arterial reconstruction procedures performed on the limbs are shown in **Table 2**. The number of successful distal bypass procedures was high in group H. Almost half of the limbs in groups N and U had undergone arterial reconstruction only in the femoro-popliteal area. One patient in group N underwent thrombectomy because of acute exacerbation of the lesion in the superficial femoral artery; however, we could not repair severe distal lesions because of the severe general condition of the patient. In all limbs of the patients in group U, more distal lesions remained because of the difficulty in treating these

Table 1 Demographic characteristics and atherosclerotic risk factors of patients, and examined SPP points

Group	H	N	U	Total	Statistical difference
Number of patients	6	6	6	18	
M:F	5:1	5:1	5:1		N.S.
Age (years)	74.6 ± 8.3	75.9 ± 6.4	69.3 ± 3.1		Between groups N and U*
Background disease					
Hypertension	4 (66.7)	4 (66.7)	5 (83.3)		N.S.
Hyperlipidemia	0	2 (33.3)	2 (33.3)		N.S.
Diabetes	4 (66.7)	6 (100)	5 (83.3)		N.S.
Ischemic heart disease	2 (33.3)	3 (50.0)	2 (33.3)		N.S.
Cerebrovascular disease	2 (33.3)	5 (83.3)	1 (16.7)		N.S.
Chronic kidney disease	3 (50.0)	4 (66.7)	5 (83.3)		N.S.
-receiving hemodialysis	2 (33.3)	3 (50.0)	4 (66.7)		N.S.
Number of limbs	6	7	6	19	
Number of examined points	13	16	16	45	

Values are expressed as means ± SD, (percentage). *Statistical analysis of age was performed using the Tukey-Kramer honestly significant difference (HSD) test.

Other analyses were performed using the Pearson chi-square test. NS: not significant

Table 2 Arterial reconstruction procedures performed for the lower limbs

Group	H	N	U
F-P lesion (failure)			
Bypass	1	2	3 (1)*
Thrombectomy	0	1*	0
Distal lesion (failure)			
Bypass	5	4	2 (1)*
PTA	0	0	1*

Values denote number of limbs.

F-P: femoro-popliteal; PTA: percutaneous transluminal angioplasty

*More distal lesions remained because of the difficulty in treating these lesions due to either calcification, stenosis or poor run-off, or the severe general conditions of the patients.

lesions due to either calcification, stenosis or poor run-off, or the severe general conditions of the patients. Failed arterial reconstruction was recognized at 5 points in 2 limbs in group U, and among the remaining 4 limbs in group U, 1 limb required minor amputation and 1 limb required major amputation, despite the patency of the reconstructed arteries. New ulcers did not occur postoperatively in any group. Rest pain disappeared in all patients in group N.

The SPP values are shown in **Table 3**. The preoperative SPP values in all groups were <30 mmHg, without a statistically significant difference. The postoperative SPP values increased by 36.9 ± 17.0 mmHg in group H

($P = 0.002$), 24.7 ± 12.0 mmHg in group N ($P < 0.0001$), and 6.6 ± 12.7 mmHg in group U (N.S.). In these groups, the actual postoperative SPP values were 57.7 ± 15.3 mmHg in group H, 46.7 ± 18.1 mmHg in group N, and 31.7 ± 16.4 mmHg in group U; the postoperative SPP value of group U was markedly lower than those of the other 2 groups. The date of postoperative examination was later in group H than in the other 2 groups.

Postoperative demographics of the numbers of limbs divided by mean SPP values in each group are shown in **Fig 1**. In group H, no limb had a mean SPP value of <30 mmHg and 83% of the limbs had a value of ≥ 40 mmHg. In group N, 57% of the limbs had a mean SPP value of

Table 3 SPP values before and after arterial reconstructions

Group	H	N	U	Statistical difference
Preoperative SPP value (mmHg)	20.8 ± 11.3	22.0 ± 8.7	25.3 ± 9.7	N.S.
Postoperative SPP value (mmHg)	57.7 ± 15.3	46.7 ± 18.1	31.7 ± 16.4	Significantly different between H and U, N and U
Date of postoperative examination (POD)	23.8 ± 13.0	13.2 ± 5.7	7.8 ± 3.4	Significantly different between H and N, H and U

Values are expressed as means ± SD. Statistical analyses were performed with the Tukey-Kramer HSD test.

NS: not significant; POD: postoperative day

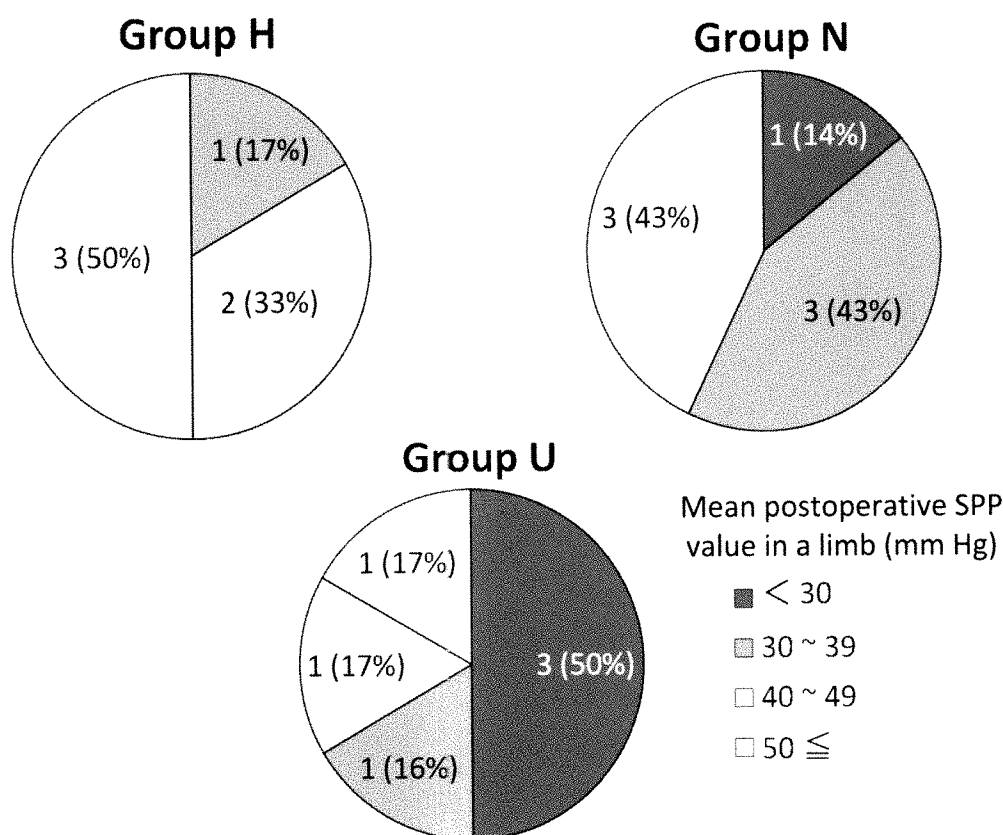


Fig. 1 Postoperative demographics of the numbers of limbs divided by the mean SPP values in each group. {number of limbs (%)}

<40 mmHg. In group U, 66% of the limbs had a mean SPP value of <40 mmHg and 50% of the limbs had a mean SPP value of <30 mmHg.

Almost all (89%) points with SPP values of <30 mmHg were in group U. For SPP values of 30–39 mmHg, group U showed a decrease of points to 33%, group N showed 56% and group H showed 11%. In SPP values of 40–49 mmHg, each of the 3 groups was nearly equivalent at 33%. Finally, only 11% of the points with SPP values of ≥50 mmHg were in group U, while 50% of the points

with SPP values of ≥50 mmHg were in group H.

DISCUSSION

In this study, we set out to assess the utility of SPP measurement in the evaluation of the outcome of vascular constructions for patients with CLI.

Regarding the backgrounds of the patients in the present study in relation to wound healing, half of the limbs of the patients in group U had undergone arterial

reconstruction in the proximal area above the knee. However, graft failure occurred in 2 limbs in this group. On the other hand, the operative results in groups H and N were acceptable, despite similar or high ratios of limbs that underwent distal bypass surgery.

The principle of arterial reconstruction is to cure the lesions successively, starting from the most proximal lesion.^{10, 11)} With reconstruction of the proximal lesion, an increase in peripheral blood perfusion can be expected even if remnants of the obliterative lesion remain on the distal side. However, the postoperative SPP values in group U indicated that postoperative perfusion was insufficient in this group. Additionally, in 2 limbs in which an increase in peripheral blood perfusion was expected in this group, the procedure resulted in arterial reconstruction failure and eventual amputation. It is possible that some patients in group U with severe lesions in the distal arteries had poor run-off, despite the success of proximal arterial reconstruction. The postoperative SPP values in group N were better than those in group U but less than those in group H. Compared with group H, group N featured more patients with chronic kidney disease and group U had even more. Additionally, groups N and U included more patients with diabetes than group H; therefore, the patients in groups N and U could have had more advanced distal lesions than did the patients in group H.¹²⁻¹⁴⁾

Previous studies have suggested a value of 30 mmHg^{1, 2, 6)} or 40 mmHg^{4, 5)} to be the critical SPP threshold necessary for wound healing. In the present study, 50% of the limbs had a mean postoperative SPP value of <30 mmHg in group U, consistent with the results of previous reports. Therefore, we considered an SPP value of <30 mmHg to indicate an unfavorable condition for wound healing. However, there was no limb in group H that showed a mean SPP value of <30 mmHg postoperatively. This reinforced our assumption that an SPP value of ≥ 30 mmHg was necessary for wound healing. On the other hand, 88% of the limbs in group H showed a mean SPP value of ≥ 40 mmHg postoperatively. Yamada et al. reported that 69% of patients with an ischemic ulcer and with an SPP value of ≥ 40 mmHg showed wound healing, and when a cut-off SPP value of 40 mmHg for wound healing was set, the sensitivity was 72% and the specificity was 88%.⁵⁾ Based on the above results, it is desirable to have a minimum SPP value of at least 30 mmHg, and ideally higher than 40 mmHg, for wound healing. In group N, SPP improved to a lesser extent than in group H; however, rest pain disappeared in all patients. It is generally known that greater blood perfusion is required to

promote wound healing than to improve rest pain. An SPP value of 30 mmHg may be the borderline for the development of rest pain.

In group U, 1 limb with postoperative SPP values of ≥ 60 mmHg in 2 points were observed. This patient had used steroids for a long period for polyneuropathy, thus the drug or the underlying disease could have negatively influenced wound healing. Another study reported a patient who required major amputation, despite showing a high SPP value, due to an uncontrolled infection in the foot.¹⁵⁾ This indicates that high SPP values do not necessarily guarantee wound healing. SPP measurement can evaluate perfusion only to a depth of about 1.5 to 2.0 mm below the skin surface. Therefore, not only SPP, but also many other factors such as muscle perfusion, oxygen partial pressure of blood, presence of infection, size of ulcer, and cellular capacity for regeneration, may influence wound healing, therefore wound healing cannot be predicted by SPP value alone. The control of all other factors is necessary to achieve wound healing.

The limitations of this study were as follows. First, the number of patients was too small to make a definitive conclusion. However, the present results add evidence supporting the usefulness of SPP examination for assessing the effects of vascular reconstruction on wound healing, although additional studies involving a larger number of patients as well as more data are needed. Second, the timing of postoperative SPP measurement was not fixed partly because of the influence of the physical condition of the patient and partly because this was a study of retrospective data, not a planned prospective study. Since all limbs were examined only once after surgery, data on changes in the SPP value over time were not available. Evaluation and comparison of SPP at a similar time would be ideal in future studies for a more appropriate comparison.

CONCLUSION

SPP measurement before and after arterial reconstruction is useful to assess improvement in tissue circulation and to predict to some extent the possibility of wound healing. In support of the findings of limited reports in the literature on the usefulness of SPP for assessing the effects of vascular reconstruction on ulcer wound healing, an SPP value of ≥ 30 mmHg is considered necessary for wound healing, but it does not guarantee it. It is desirable to have a minimum SPP value of 30 mmHg and ideally greater than 40 mmHg to achieve wound healing.

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DISCLOSURE STATEMENT

The authors declare that they have no conflicts of interest associated with this study.

REFERENCES

- 1) Castronuovo JJ, Adera HM, Smiell JM, et al. Skin perfusion pressure measurement is valuable in the diagnosis of critical limb ischemia. *J Vasc Surg* 1997; **26**: 629-37.
- 2) Lo T, Sample R, Moore P, et al. Prediction of wound healing outcome using skin perfusion pressure and transcutaneous oximetry: a single-center experience in 100 patients. *Wounds* 2009; **21**: 310-6.
- 3) Miyashita Y, Saito S, Miyamoto A, et al. Cilostazol increases skin perfusion pressure in severely ischemic limbs. *Angiology* 2011; **62**: 15-7.
- 4) Urabe G, Yamamoto K, Onozuka A, et al. Skin perfusion pressure is a useful tool for evaluating outcome of ischemic foot ulcers with conservative therapy. *Ann Vas Dis* 2009; **2**: 21-6.
- 5) Yamada T, Ohta T, Ishibashi H, et al. Clinical reliability and utility of skin perfusion pressure measurement in ischemic limbs - Comparison with other noninvasive diagnostic methods. *J Vasc Surg* 2008; **47**: 318-23.
- 6) Adera HM, James K, Castronuovo JJ Jr, et al. Prediction of amputation wound healing with skin perfusion pressure. *J Vasc Surg* 1995; **21**: 823-8.
- 7) Shimazaki M, Matsuki T, Yamauchi K, et al. Measurement of skin perfusion pressure in hemodialyzed patients: Association with toe/brachial index. *Dialysis & Transplantation* 2008; **37**: 431-8.
- 8) Kawarada O, Yokoi Y. Native chronic total occlusion recanalization after lower limb bypass graft occlusion: a series of nine cases. *Catheter Cardiovasc Interv* 2010; **76**: 214-9.
- 9) Iida O, Nanto S, Uematsu M, et al. Importance of the angiosome concept for endovascular therapy in patients with critical limb ischemia. *Catheter Cardiovasc Interv* 2010; **75**: 830-6.
- 10) Hirsch AT, Haskal ZJ, Hertzner NR, et al. ACC/AHA 2005 practice guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic)--A collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery,* Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients with Peripheral Arterial Disease). *Circulation* 2006; **113**: E463-E654.
- 11) Norgren L, Hiatt WR, Dormandy JA, et al. Inter-society consensus for the management of peripheral arterial disease (TASC II). *J Vasc Surg* 2007; **45**: S5-S67.
- 12) Hoshino J, Fujimoto Y, Naruse Y, et al. Characteristics of revascularization treatment for arteriosclerosis obliterans in patients with and without hemodialysis. *Circ J* 2010; **74**: 2426-33.
- 13) Kimura H, Miyata T, Sato O, et al. Infrainguinal arterial reconstruction for limb salvage in patients with end-stage renal disease. *Eur J Vasc Endovasc Surg* 2003; **25**: 29-34.
- 14) Ramdev P, Rayan SS, Sheahan M, et al. A decade experience with infrainguinal revascularization in a dialysis-dependent patient population. *J Vasc Surg* 2002; **36**: 969-74.
- 15) Komoda T. Study on the usefulness of skin perfusion pressure (SPP) in patients with foot lesions. *J Jpn PRS* 2009; **29**: 73-82.

► Case Report ◀

Atypical Giant Cell Arteritis Presenting as Lack of a Pulse in the Upper Extremity

Shintaro Shibutani, MD, PhD,¹ Hideaki Obara, MD, PhD,² Shigenao Kan, MD, PhD,³ Shin Takahashi, MD, PhD,³ Kenji Ogawa, MD, PhD,⁴ and Yuko Kitagawa, MD, PhD²

Giant cell arteritis (GCA), an inflammatory vasculopathy that preferentially affects medium-sized and large arteries, has diverse symptoms and varied clinical courses that can make the diagnosis difficult. We describe a 75-year-old woman in whom GCA presented as lack of a pulse in the right arm. Although steroid therapy is generally effective for treating GCA, surgical intervention provides a biopsy specimen for a definitive diagnostic study and restores blood flow in the affected limb. GCA should be considered along with atherosclerosis in cases of occlusive disease of the upper extremity, especially if the patient is an elderly woman.

Key words: giant cell arteritis, pulseless disease, arm ischemia

INTRODUCTION

Giant cell arteritis (GCA) is a chronic vasculitis of large and medium-sized arteries.¹⁾ It most often affects the superficial temporal artery, although facial, carotid, myometrial, and upper and lower limb arteries may also be involved. We describe a case of GCA presenting as lack of a pulse in the upper extremity.

CASE REPORT

A 75-year-old woman was referred to our institution with symptom of the right arm claudication for several

weeks. She had general fatigue and had lost 5 kg of body weight. She had no fever, temporal or occipital headache, scalp tenderness, jaw or tongue claudication, respiratory tract or musculoskeletal manifestations, or visual disturbances. She had no past medical history such as trauma or radiotherapy and family history. The patient did not have any of the usual risk factors for atherosclerosis: smoking, hypercholesterolemia, hypertension, or diabetes mellitus.

On examination, the patient's right hand was observed to be pale and cool, and there was no distal pulse in the right upper extremity. The systolic blood pressure was 40 mmHg on the right radial artery. The temporal arteries were palpable on both sides. Laboratory tests showed normal renal and liver function tests while showing elevated erythrocyte sedimentation rate (ESR) of 108 mm/hour, C-reactive protein (CRP) level of 2.5 mg/L and moderate anemia (hemoglobin level, 10.1 g/dL). Assessments for rheumatoid factor and antinuclear antibody and antineutrophil cytoplasmic antibody yielded negative results.

A chest radiograph and computerized tomographic study showed no evidence of cervical ribs, chronic aortic dissection, or other abnormalities. Selective digital subtraction angiography (DSA) revealed severe localized smooth stenosis of the right brachial artery (Fig. 1). No other stenotic or atherosclerotic changes were observed.

¹Department of Vascular surgery, Kawasaki Municipal Hospital, Kawasaki, Kanagawa, Japan

²Department of Surgery, Keio University School of Medicine, Shinjuku-ku, Tokyo, Japan

³Department of Surgery, Nippon Kokan Hospital, Kawasaki, Kanagawa, Japan

⁴Department of Radiology, Nippon Kokan Hospital, Kawasaki, Kanagawa, Japan

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Corresponding author: Shintaro Shibutani, MD, PhD. Department of Vascular Surgery, Kawasaki Municipal Hospital, 12-1 Shinkawadori, Kawasaki-ku, Kawasaki, Kanagawa 210-0013, Japan

Tel: +81-44-233-5521, Fax: +81-44-245-9600

E-mail: shibutani@kmh.gr.jp



Fig 1 Selective digital subtraction angiogram showing severe localized stenosis of the right brachial artery.

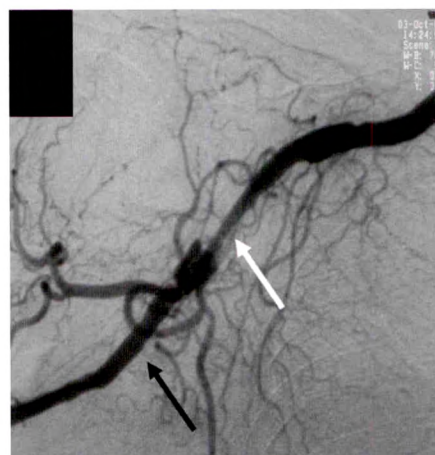


Fig 2 Selective digital subtraction angiogram showing patent saphenous vein graft (black arrow) and a new stenotic lesion on the proximal section of the brachial artery (white arrow).

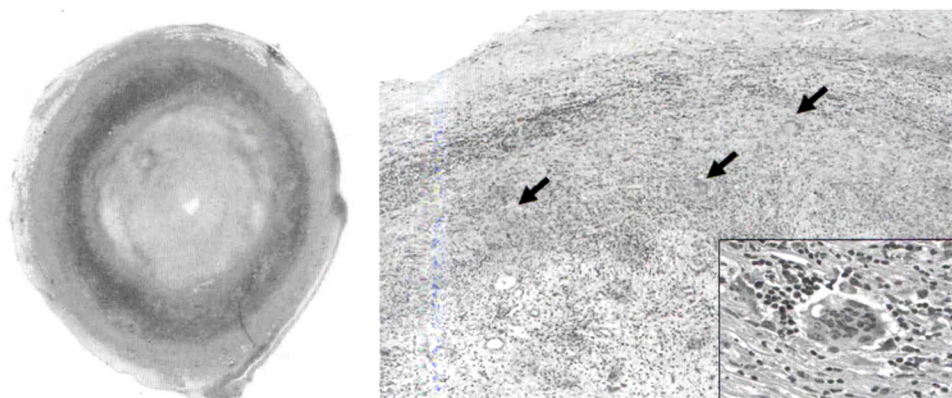


Fig 3 Photomicrograph of resected specimen of the right brachial artery showing extensive narrowing of the lumen. High-power microscopical view of inflammatory zone showing infiltration of lymphocytes and multinucleated giant cells (arrow). (Hematoxylin and eosin stain, $\times 200$)

We decided to perform surgery on the purposes of pathologic confirmation of the arterial lesion and restoration of the blood flow. Under local anesthesia, the stenotic segment of the right brachial artery was resected and restored blood flow by the interposition graft with autologous saphenous vein.

After the operation, the patient's malaise resolved, and her hand became warm. The systolic blood pressure in the radial artery returned to normal (140 mmHg on both sides). On the other hand, she continued to complain of general fatigue. A week postoperatively, selective DSA showed that the saphenous vein graft was patent but that there was a new stenotic lesion in the proxi-

mal segment of the brachial artery (**Fig. 2**). A histologic evaluation of the previously resected brachial artery specimen showed infiltration of the lymphocytes and multinucleated giant cells throughout the arterial wall suggesting GCA (**Fig. 3**).

Steroid therapy was started, with 50 mg of prednisone given daily for two weeks and subsequent gradual tapering of the daily dose by 5 mg every two weeks. Her condition including general fatigue improved with the CRP level of less than 0.5 mg/L and the ESR level of less than 50 mm/hour. Selective DSA one month later showed resolution of the new stenotic lesion that was suspected to be GCA.

DISCUSSION

GCA is an inflammatory vasculopathy that preferentially affects medium-sized and large arteries.¹⁾ The most frequently affected vessels are the branches of the external carotid artery, including the posterior ciliary arteries that supply the optic nerve. Inflammation of the aorta and its branches in the upper extremity can occur but is found in only a subset of patients. The subclavian and axillary arteries are the proximal aortic branches most commonly affected and 1%–2% of patients of GCA may present predominately with arm claudication.²⁾ Thus, it is important to avoid attributing all occlusive arterial disease in older patients to atherosclerosis because some may have GCA.

GCA has a wide spectrum of clinical manifestations related to both systemic inflammation and ischemia.¹⁾ Although there are no novel laboratory markers for the definite diagnosis of GCA, most patients with GCA have an elevated ESR. The American College of Rheumatology has included this marker in the criteria for classifying GCA. However, up to 23% of patients with GCA have a normal ESR.³⁾ Therefore, the finding of a normal ESR is not incompatible with the diagnosis of active GCA. The level of CRP has been observed to be a more sensitive indicator of disease activity than ESR, both at diagnosis and during relapse.⁴⁾ In our case, although the patient had some systemic manifestation and high level of ESR, she lacks ischemic manifestation of the cranial arteries such as headache and jaw claudication. After experiencing an atypical case of GCA affecting upper extremity artery, we would like to recommend GCA should be put in the list of differential diagnosis in patients complaining of upper extremity claudication, particularly in patients with some systemic manifestation and elevated ESR or CRP.

Positive results on a biopsy evaluation of the temporal artery provide confirmation of the diagnosis of GCA. Several noninvasive methods for diagnosing the disorder have been investigated, including color Doppler sonography and magnetic resonance imaging. However, although these techniques provide information about the widespread nature of GCA, none has replaced the temporal artery biopsy for diagnosis. Local signs and symptoms of temporal artery involvement may be absent in some patients, but a biopsy of the vessel yields positive results in about 80% of such patients.⁵⁾ On the other hand, Brack et al.⁶⁾ reported that temporal artery biopsy yielded nega-

tive results in 42% of patients with large-vessel GCA. Tarnoff et al.⁷⁾ reported a case of bilateral superficial femoral GCA in which a postoperative histologic assessment of the superficial femoral arteries confirmed the diagnosis, whereas a temporal artery biopsy had negative results. In our case, the diagnosis was confirmed by a histological study of the resected brachial artery specimen, so a temporal artery biopsy was not done.

Surgical intervention to alleviate ischemic symptoms in an extremity of a patient with GCA is rarely necessary, but a variety of techniques has been described, including implantation of saphenous vein or Dacron grafts and endarterectomy.⁸⁾ In general, however, attempts at vascular reconstruction for peripheral arterial involvement in GCA have been disappointing. In our case, we performed surgery to obtain a specimen for a histological evaluation of the stenotic lesion and to restore blood flow because we considered the patient to be at low risk of operative complications. In most cases of GCA, treatment with high doses of corticosteroids dramatically suppresses the signs of systemic inflammation, and in some cases, blood flow can be restored by use of immunosuppression alone.⁹⁾ In suspected cases of GCA, beginning steroid treatment before performing a temporal artery biopsy to confirm the diagnosis may be justified to prevent complications from the disease. In our case, the improvement in the lesion in the proximal brachial artery after steroid therapy was initiated suggests that if such treatment had been administered before the operation, the initial lesion may have resolved. With respect to the use of minimally invasive procedures to restore blood flow in cases of GCA, Amann-Vesti et al.¹⁰⁾ reported that balloon angioplasty was effective in treating occlusive lesions in GCA patients with severe vascular symptoms that persisted despite immunosuppressive therapy.

In conclusion, the diagnosis is difficult to make because of the diverse symptoms and varied course of GCA. Large-vessel GCA has distinct clinical manifestations and often occurs without involvement of the cranial arteries. The diagnosis of GCA should be considered in some cases of occlusive disease of the upper extremity, especially if the patient is an elderly woman. Steroid therapy is generally effective for treating GCA. When the stenotic lesion is located in the upper extremity and arterial short segment, as it was in our patient, surgery is useful for confirming the diagnosis and restoring blood flow.

REFERENCES

- 1) Salvarani C, Cantini F, Boiardi L, Hunder GG. Polymyalgia rheumatica and giant-cell arteritis. *N Engl J Med* 2002; **347**: 261-71.
- 2) Klein RG, Hunder GG, Stanson AW, Sheps SG. Large artery involvement in giant cell (temporal) arteritis. *Ann Intern Med* 1975; **83**: 806-12.
- 3) Salvarani C, Hunder GG. Giant cell arteritis with low erythrocyte sedimentation rate: frequency of occurrence in a population-based study. *Arthritis Rheum* 2001; **45**: 140-5.
- 4) Cantini F, Salvarani C, Olivieri I, Macchioni L, Ranzi A, Niccoli L, et al. Erythrocyte sedimentation rate and C-reactive protein in the evaluation of disease activity and severity in polymyalgia rheumatica: a prospective follow-up study. *Semin Arthritis Rheum* 2000; **30**: 17-24.
- 5) Walz-Leblanc BA, Ameli FM, Keystone EC. Giant cell arteritis presenting as limb claudication. Report and review of the literature. *J Rheumatol* 1991; **18**: 470-2.
- 6) Brack A, Martinez-Taboada V, Stanson A, Goronzy JJ, Weyand CM. Disease pattern in cranial and large-vessel giant cell arteritis. *Arthritis Rheum* 1999; **42**: 311-7.
- 7) Tarnoff JF, Pearlman E, Balkoura MH, Venkataraman M. Bilateral superficial femoral giant cell arteritis. *J Cardiovasc Surg (Torino)*. 1990; **31**: 375-9.
- 8) Halpin DP, Moran KT, Jewell ER. Arm ischemia secondary to giant cell arteritis. *Ann Vasc Surg*. 1988; **2**: 381-4.
- 9) Lambert M, Weber A, Boland B, De Plaen JF, Donckier J. Large vessel vasculitis without temporal artery involvement: isolated form of giant cell arteritis? *Clin Rheumatol* 1996; **15**: 174-80.
- 10) Amann-Vesti BR, Koppensteiner R, Rainoni L, Pfammatter T, Schneider E. Immediate and long-term outcome of upper extremity balloon angioplasty in giant cell arteritis. *J Endovasc Ther* 2003; **10**: 371-5.

Case Report

Complete Rupture of Polytetrafluoroethylene-covered Endoprosthesis after Exclusion of a Popliteal Aneurysm

Issam Abouliatim, MD, Khaoula El Alaoui, MD, Marec Majewski, MD, and Jean-pierre Becquemin, MD

Popliteal artery aneurysm (PAA) is the most commonly reported peripheral artery aneurysm. The usual treatment is exclusion bypass with a saphenous vein. However, the availability of medium size covered stent graft is an attractive option. By performing this procedure percutaneously, we can shorten the hospital stay of the patient. Favourable early and long-term results have been reported; however, little is known about the durability of the procedure. Given the mobile location of the stent-graft close to the knee joint, graft damage can be expected. We describe a case of complete rupture of a Viabahn® endoprosthesis which was inserted to exclude a PAA.

Key words: viabahn endoprosthesis, type III endoleak, popliteal aneurysm

CASE REPORT

A 60-years-old man with a history of hypertension and hypercholesterolemia and no associated disease complained of knee pain. He had been still working and practicing sports. Vascular investigations revealed a fusiform and subarticular popliteal aneurysm, 37 mm in diameter (Fig. 1A) and 40 mm in length (Fig. 1B), with a mural thrombus and three patent crural vessels (Fig. 1C). Because the patient had refused the bypass procedure, an endovascular treatment was chosen. Under local anaesthesia, a covered Viabahn® stent (8 mm × 100 mm) (W.L. Gore & Associates, Inc., Flagstaff, Arizona, USA) was inserted via an ipsilateral percutaneous femoral puncture. Control colour duplex ultrasound at 1 and 9 months showed no endoleak and confirmed the patency of the stent. At 12 months, the patient had no complaint, but the colour duplex ultrasound and computed tomography

(CT)-scan showed a large endoleak with an aneurysm perfusion. The mechanism of the leak was thought to be related to fracture of the stent and complete tear in the polytetrafluoroethylene (PTFE) membrane at the level of the articular interline (Fig. 2). We attempted to provide clear information about this infrequent complication already described in active patients. However, the patient still refused the bypass procedure as he was asymptomatic. A redo stenting was then successfully performed with the same device (Viabahn® stent (8 mm × 100 mm)).

DISCUSSION

The Viabahn® endoprosthesis (W.L. Gore & Associates, Inc., Flagstaff, Arizona, USA), which is a modified version of Hemobahn®, is a self-expandable stent; it consists of an ultra-thin lining of PTFE and an external support of nitinol (NiTi = nickel : titanium) extending the length of the PTFE to confer this great flexibility.

Despite its properties, fractures of the nitinol support of Hemobahn/Viabahn endoprostheses have been described, but complete rupture with both the stent fracture and tear of the PTFE is rare.¹⁻³ In these two studies, complete rupture was not described as so, even though a leak re-feeding of the aneurysm was reported. Moreover, no imaging evidence has been reported in order to demonstrate the type III leakage. The first case was about an

Department of Vascular Surgery, Henri Mondor Hospital, University Paris 12, Creteil, France

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Corresponding author: Issam Abouliatim, MD. Department of Vascular Surgery, Henri Mondor Hospital, University Paris 12, 51, av du Marechal de Lattre de Tassigny, 94000 Creteil, France
Tel: +33-610159295, Fax: +33-149814927
E-mail: i_abouliatim@hotmail.com

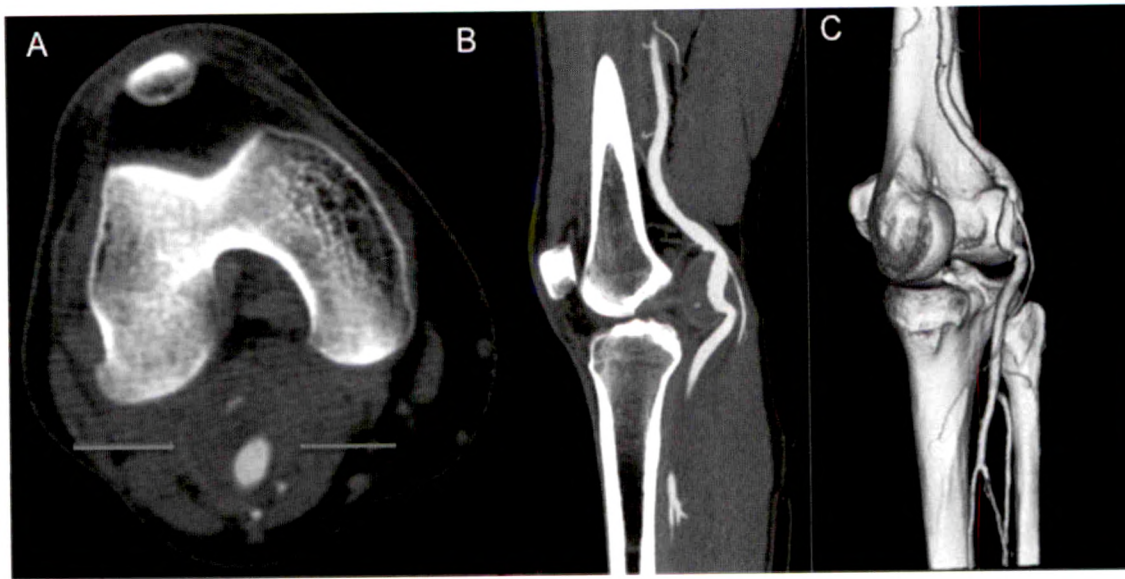


Fig. 1 CT scan revealed a fusiform and subarticular popliteal aneurysm.
A: Axiale view of the popliteal aneurysm (arrows).
B: Sagittal view showed the length of the aneurysm and the mural thrombus.
C: Volume rendering image showed patent leg arteries.
 CT: computed tomography

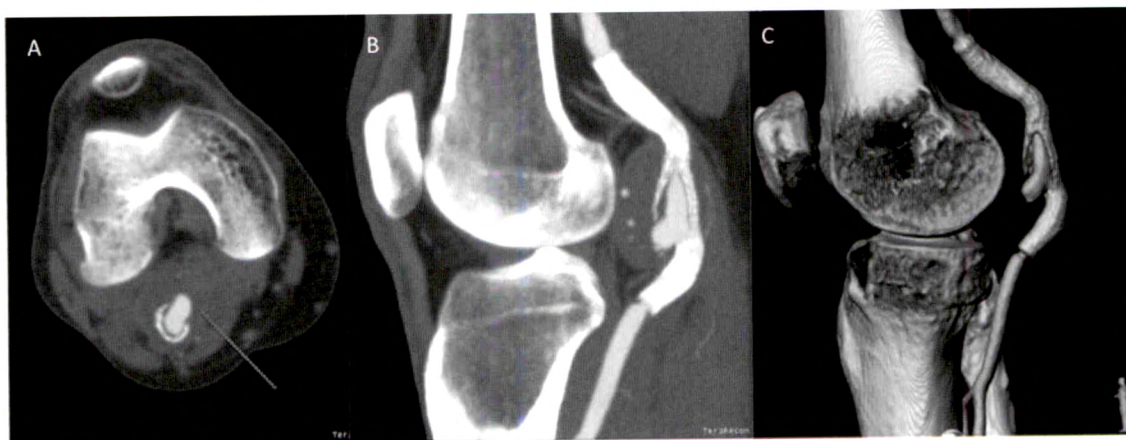


Fig. 2 CT scan revealed a complete rupture of a covered Viabahn® stentgraft.
A: Axial view showed the rupture of the covered stent and direct injection of the contrast media within the aneurysmal sac (arrow), suggesting type III endoleak.
B: Sagittal view of MPR image showed that the start of the rupture was situated exactly at the level of the supracondylar tubercle.
C: Volume rendering image showed that the stent followed an angulation precisely to the proximal part of the femoral condyles.
 CT: computed tomography

endoleak between two stents at the overlapping zone: the second case was supposed to be related to the fracture stent associated with a refilling of the aneurysm but authors have been provided any evidences of a direct injection of the aneurysmal sac from the prosthesis. The incidence of Nitinol fractures is probably underestimated

because systematic radiography of the knee is not part of the follow-up protocol.¹⁾ However, this does not apply to complete rupture of the PTFE, because colour duplex ultrasound and/or CT scan are carried out during follow-up in order to detect endoleaks.^{1, 2)}

Only one case of complete rupture of Hemobahn stent

has been reported with peroperative visual identification of fabric torn. As described by Koelemay et al., three months after insertion of a single Hemobahn stent to exclude iterative false aneurysm of the distal anastomosis of a subarticular femoropopliteal bypass; it was attributed, in part, to balloon dilation of the proximal end of the stent and to mechanical constraints due to movements of the knee.²⁾ In the study of Tielliu et al.,¹⁾ the rate of fracture and rupture of stents at 5 and 10 years follow-up was 78% and 73%, respectively; risk factors included young age (mean, 61 years) and multiplicity of stents. The most common site of these incidents was the overlapping zone in 93.3% of cases and, more precisely, the supracondylar tubercle in 73.3%.¹⁾ It is interesting to note that in our 60-year-old patient, the start of the rupture was situated exactly at the level of the supracondylar tubercle (**Fig. 2A and 2B**).

During flexion of the knee, the point of maximal angulation of the popliteal artery is level with the supraarticular portion of the artery at the superior margin of the femoral condyles. In our patient and in full view of **Fig. 1C and 2C**, we could speculate that the angulation of the stent already marked will be even more important after knee flexion. This maximal zone constraints are situated 2–3 cm above the articular interline.^{3,4)}

According to Midy et al.⁵⁾ there are two unfavourable anatomic criteria for insertion of a popliteal endoprosthesis: the excessive tortuosity of the artery and distal spread of the aneurismal process, prompting the need for several endoprostheses and then increasing the risk of fracture of the Nitinol at the overlapping zones.

Stent fractures usually occur in young people, probably because they are more active.¹⁾ Wensing et al.⁶⁾ showed that changes in the morphology of the femoropopliteal artery occur depending on age. In patients < 30 years of age with a bent knee, minor arterial tortuosities have been noted above the adductor hiatus. In contrast, in patients > 45 years of age, one or more tortuosities have been noticed below the hiatus. In patients > 60 years of age, the tortuosities do not disappear on extension of the knee. We could speculate, in those patients, that the

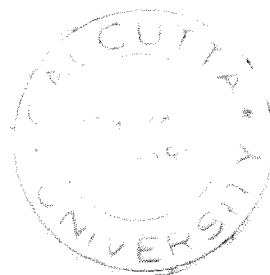
angulation of the stent will be marked in extension and will be more important after flexion. Indeed, the range of motion of the knee, which depends on the activity, can favor stent shear stress. This enables the placement of covered stents in young subjects who must then be followed closely due to the increased risk of rupture with age.

CONCLUSION

This case highlights the importance of monitoring with colour duplex ultrasound and/or CT scan after using the Viabahn® device. One can speculate that the matrix of the stent and the PTFE of prosthesis are subjected to important mechanical stress especially at the level of popliteal artery.

REFERENCES

- 1) Tielliu IF, Zeebregts CJ, Vourliotakis G, Bekkema F, van den Dungen JJ, Prins TR, et al. Stent fractures in the Hemobahn/Viabahn stent graft after endovascular popliteal aneurysm repair. *J Vasc Surg* 2010; **51**: 1413-8.
- 2) Koelemay MJ, Rijcken TH. Fracture of a covered stent used for pseudoaneurysm exclusion in a prosthetic femoro-infrapopliteal bypass. *J Endovasc Ther* 2008; **15**: 375-8.
- 3) Curi MA, Geraghty PJ, Merino OA, Veeraswamy RK, Rubin BG, Sanchez LA, et al. Mid-term outcomes of endovascular popliteal artery aneurysm repair. *J Vasc Surg* 2007; **45**: 505-10.
- 4) Jung E, Jim J, Rubin BG, Sanchez LA, Choi ET, Sicard GA, et al. Long-term outcome of endovascular popliteal artery aneurysm repair. *Ann Vasc Surg* 2010; **24**: 871-5.
- 5) Midy D, Berard X, Ferdani M, Alric P, Brizzi V, Ducasse E, et al. AURC French University Association for Vascular Surgery. A retrospective multicenter study of endovascular treatment of popliteal artery aneurysm. *J Vasc Surg* 2010; **51**: 850-6.
- 6) Wensing PJ, Scholten FG, Buijs PC, Hartkamp MJ, Mali WP, Hillen B. Arterial tortuosity in the femoropopliteal region during knee flexion: a magnetic resonance angiographic study. *J Anat* 1995; **187**: 133-9.



» Case Report «

Two-stage Surgery for Double Infected Aneurysms in the Infrarenal Abdominal and Descending Thoracic Aorta

Kosaku Nishigawa, MD, Atsushi Tabuchi, MD, Hiroki Takiuchi, MD, Hiroshi Kubo, MD, Hisao Masaki, MD, and Kazuo Tanemoto, MD

A 61-year-old man complaining of lumbago and high-grade fever was admitted to our institution. Computed tomography (CT) revealed a saccular aneurysm in the infrarenal abdominal aorta and blood culture results were positive for *Streptococcus pneumoniae*. He was diagnosed with infected abdominal aortic aneurysm, and antibiotic therapy was initiated. Follow-up CT demonstrated a rapidly-enlarging abdominal aortic aneurysm and a newly-developed descending thoracic aortic aneurysm. For this case, two-stage surgery consisting of extra-anatomical bypass and in-situ reconstruction using rifampicin-soaked Dacron graft was performed after an interval of 37 days. The patient was discharged 14 days after the second surgery without any complications.

Key words: infected aortic aneurysm, multiple aneurysms, rifampicin-soaked graft

INTRODUCTION

Infected aortic aneurysm is a relatively rare but fatal vascular disease; therefore, surgical intervention is indispensable for most cases. The optimal timing of surgery and the choice of procedures are controversial, especially in cases with multiple infected aortic aneurysms, which are extremely rare. Herein, we describe a successful surgical case of double infected aneurysms in the infrarenal abdominal and descending thoracic aorta treated by two-stage surgery consisting of extra-anatomical bypass with the radical aneurysmectomy of the abdominal aorta and replacement of the descending aorta using a rifampicin-soaked gelatin-sealed Dacron graft.

Department of Cardiovascular Surgery, Kawasaki Medical School, Kurashiki, Okayama, Japan

Received: March 6, 2011; Accepted: April 24, 2011
Corresponding author: Kosaku Nishigawa, MD, Department of Cardiovascular Surgery, Kawasaki Medical School, 577 Matsushima, Kurashiki, Okayama 701-0192, Japan
Tel: +81-86-462-1111, Fax: +81-86-464-1189
E-mail: nippie550102@yahoo.co.jp

CASE REPORT

A 61-year-old man was admitted to our institution with the chief complaint of lumbago and high-grade fever. On admission, his vital signs were normal, including a body temperature of 36.7 degrees. Laboratory data showed a white blood cell count of $13160/\text{mm}^3$ and C-reactive protein (CRP) of 37.65 mg/dl. Enhanced computed tomography (CT) at the time of admission revealed a saccular aneurysm in the infrarenal abdominal aorta, measuring 46 mm in diameter with surrounding inflammation (**Fig. 1A**). Blood culture results were positive for *Streptococcus pneumoniae*. Based on these findings, the aneurysm was diagnosed as infected, and intravenous administration of antibiotics was promptly started. However, the laboratory data did not improve, and a follow-up CT performed 6 days after admission demonstrated not only a rapidly-enlarging abdominal aortic aneurysm measuring a maximum diameter of 56 mm (**Fig. 1B**) but also a newly-developed, lobulated aneurysm in the descending aorta (**Fig. 2A**). Therefore, we concluded that surgical intervention should be performed for these aneurysms and decided to intervene the aneurysm in the abdominal aorta prior to the aneurysm in the descending aorta.

Firstly, we performed the axillo-bifemoral bypass

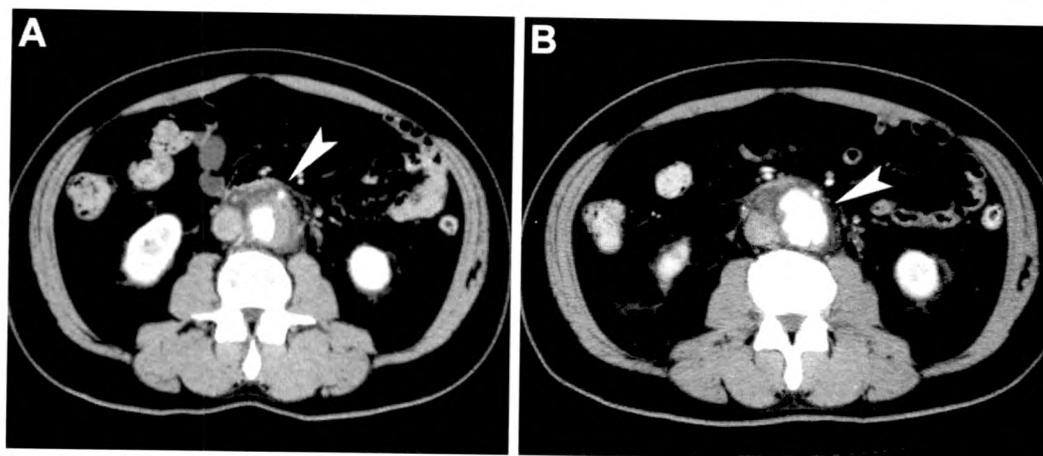


Fig. 1 A: Enhanced computed tomography (CT) scan at the time of admission revealed a saccular aneurysm in the infrarenal abdominal aorta, measuring 46 mm in diameter with surrounding inflammation (arrowhead).
B: Follow-up CT performed 6 days after admission demonstrated a rapidly-enlarging lobulated aneurysm measuring a maximum diameter of 56 mm (arrowhead).

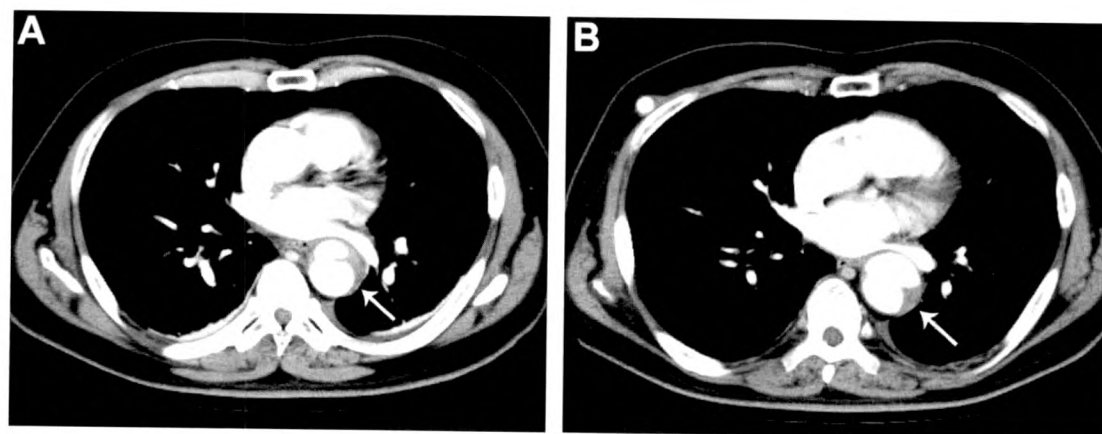


Fig. 2 A: Enhanced computed tomography (CT) scan performed 6 days after admission demonstrated a newly-developed lobulated aneurysm in the descending aorta (arrow).
B: Follow-up CT performed 18 days after the initial surgery showing an aneurysm in the descending aorta enlarged to the diameter of 48 mm (arrow).

using the rifampicin-soaked gelatin-sealed knitted Dacron graft (Gelsoft plus; Vascutek, Renfrewshire, Scotland) prior to the midline laparotomy. Then the retroperitoneum was opened to expose the aneurysm. The infrarenal abdominal aorta and bilateral common iliac artery were clamped, and the aneurysm was opened to identify an abscess formation. Subsequently, the aneurysmal wall was completely resected with contiguous tissue; then, the aortic and bilateral iliac stumps were suture-closed using autologous fascial pledget. Both stumps were covered with the omental flap after pulsative irrigation of the retroperitoneal space.

Although the patient required thrombectomy for the thrombotic occlusion of the prosthetic graft on the operative day, his postoperative recovery was uneventful. The CRP level gradually decreased to 1.6 mg/dl. However, CT re-examination performed on 18th postoperative day demonstrated that the aneurysm in the descending aorta had progressed to the diameter of 48 mm (**Fig. 2B**). We performed the second surgery for the aneurysm 37 days after the initial operation.

With the patient in a right semilateral position, his chest cavity was entered through a left thoracotomy over the 5th intercostal space. Since his abdominal aorta was

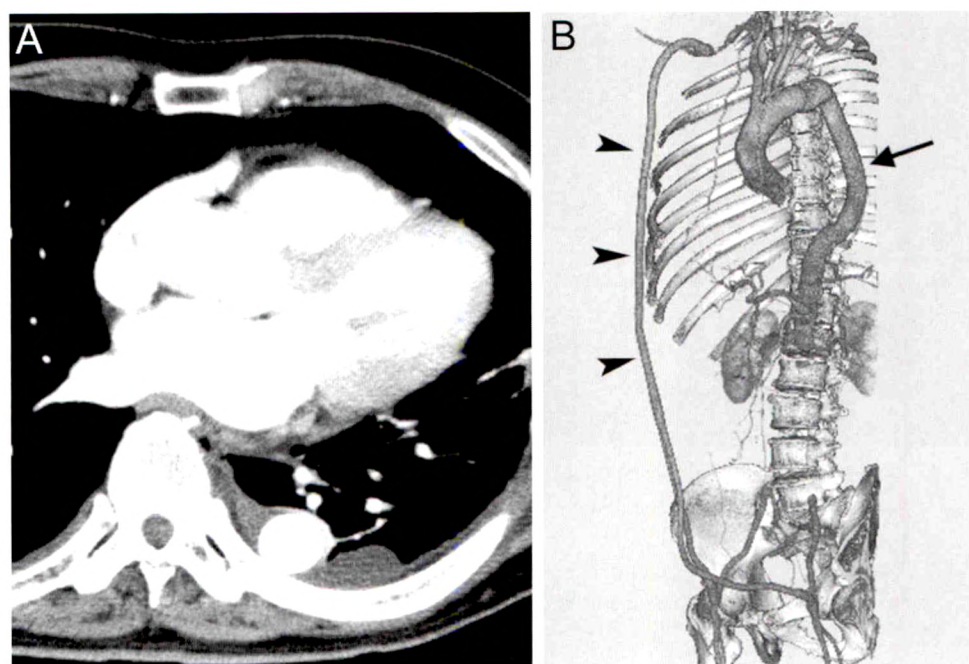


Fig. 3 Postoperative computed tomography (CT) scan findings.
A: CT scan showing successful replacement of the descending aorta, without findings of persistent or recurrent infection.
B: Three-dimensional CT scan showing a prosthetic graft of the descending aorta (arrow) and the patent axillo-bifemoral bypass graft (arrowheads).

completely resected at the initial surgery, extracorporeal circulation with the femoro-femoral bypass could not be established. Therefore, the distal aortic arch and descending aorta just above the diaphragm were chosen for drainage and return of the oxygenated blood, respectively. Thus, aorto-aortic temporary bypass was established. The aneurysm and the adjacent inflamed tissue were radically resected, and the descending aorta was replaced with the rifampicin-soaked gelatin-sealed woven Dacron graft (Gelweave: Vascutek). There were no signs of active infection, including the abscess formation. The prosthetic graft was then placed to detour around the infected field.

There were no postoperative complications. The postoperative CT scan demonstrated no signs of persistent or recurrent infection and the patent axillo-bifemoral bypass graft (**Fig. 3**). The patient was discharged from our institution 14 days after the second surgery.

DISCUSSION

Despite the progression of medical and surgical management for patients with vascular disease, infected aneurysms still remain as challenging disorder for vascular surgeons to treat with high incidence of arterial rupture

and recurrent infection. Specifically, infected aortic aneurysms are life-threatening disease, and the reported hospital mortality ranges from 16%–44%.¹⁾ Although radical debridement of all the infected tissues, including the arterial wall, as well as the administration of appropriate antibiotics, is essential for the treatment of infected aneurysm, the optimal timing and appropriate procedure to treat are controversial. In the present case, antibiotic therapies for infected infrarenal abdominal aortic aneurysm were not effective, and the infected aneurysm in the descending aorta had newly developed refractory to these treatments. We planned a two-stage surgery to treat the uncontrolled infectious state due to active infected abdominal aortic aneurysm prior to the surgery for thoracic aorta. Simultaneous surgery is considered to be too invasive and contain a potential risk of paraplegia.

Two surgical options are available for the treatment of infected abdominal aortic aneurysm: extra-anatomical bypass and in-situ reconstruction.^{2, 3)} We usually perform extra-anatomical bypass for cases with high fever, leukocytosis, elevated CRP level, or septic state refractory to antibiotic treatment, like the present case. While this procedure has the advantage of grafting via an aseptic route, the disadvantages are risk of aortic stump blowout and

axillo-bifemoral bypass graft infection.⁴⁾ For the prevention of such fatal complications, we performed suture-close of the aortic stump with reinforcement using the autologous fascial pledget and omental coverage of the stump after pulsative irrigation of the retroperitoneal space in this case. In addition, we used the rifampicin-soaked gelatin-sealed Dacron graft for axillo-bifemoral bypass. Recent studies show the satisfactory outcomes of in-situ reconstruction,⁵⁻⁸⁾ and this procedure also can be an effective surgical alternative for the treatment of primary infected abdominal aortic aneurysm. Rifampicin-soaked graft^{5, 6)} or polytetrafluoroethylene graft⁷⁾ is an available conduit for the prevention of postoperative graft infection.

On the other hand, when the infected aneurysm is located in the thoracic aorta, it is anatomically difficult to perform an extra-anatomical bypass.⁹⁾ For this reason, elective surgery in the controlled infectious phase is ideal for patients with infected thoracic aortic aneurysm. In the present case, we performed in-situ reconstruction during the subclinical infectious phase following the initial operation. We routinely perform in-situ reconstruction using a rifampicin-soaked Dacron graft with the omental coverage for the prevention of graft infection. However, we could not perform the omental coverage in this case since the omentum had already been used in the initial operation. Therefore, we placed the prosthetic graft to detour around the infected field after sufficient irrigation of the left thoracic cavity. Although the homograft is known to be better with regard to prevention of bacterial colonization than the prosthetic graft,¹⁰⁾ a homograft is not easily obtainable under the present medical system in Japan; in addition, this biological conduit is not available in our institution.

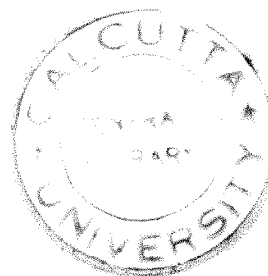
CONCLUSION

We have presented a rare case of double infected aneurysms in the infrarenal abdominal and descending tho-

racic aorta successfully treated by two-stage surgery consisting of extra-anatomical bypass and in-situ reconstruction using the rifampicin-soaked Dacron graft. Performing the appropriate procedure for the infectious phase in cases with multiple infected aortic aneurysms is of the utmost importance.

REFERENCES

- 1) N Sekar. Primary aortic infections and infected aneurysms. *Ann Vasc Dis* 2010; **3**: 24-7.
- 2) Pasic M. Mycotic aneurysm of the aorta: Evolving surgical concept. *Ann Thorac Surg* 1996; **61**: 1053-4.
- 3) Fichelle JM, Tabet G, Cormier P, et al. Infected infrarenal aortic aneurysms: when is in situ reconstruction safe? *J Vasc Surg* 1993; **17**: 635-45.
- 4) Reddy DJ, Shepard AD, Evans JR, et al. Management of infected aortoiliac aneurysms. *Arch Surg* 1991; **126**: 873-8.
- 5) Gupta AK, Bandyk DF, Johnson BL. In situ repair of mycotic abdominal aortic aneurysms with rifampin-bonded gelatin-impregnated Dacron grafts: a preliminary case report. *J Vasc Surg* 1996; **24**: 472-6.
- 6) Bandyk DF, Novotney ML, Johnson BL, et al. Use of rifampin-soaked gelatin-sealed polyester grafts for in situ treatment of primary aortic and vascular prosthetic infections. *J Surg Res* 2001; **95**: 44-9.
- 7) Kwon TW, Kim HK, Moon KM, et al. In situ polytetrafluoroethylene graft bypass for primary infected aneurysm of the infrarenal abdominal aorta. *World J Surg* 2010; **34**: 1689-95.
- 8) Maeda H, Umezawa H, Goshima M, et al. Primary Infected abdominal aortic aneurysm: Surgical procedures, early mortality rates, and a survey of the prevalence of infectious organisms over a 30-year period. *Surg Today* 2011; **41**: 346-51.
- 9) Muller BT, Wegener OR, Grabitz K, et al. Mycotic aneurysms of the thoracic and abdominal aorta and iliac arteries: experience with anatomic and extra-anatomic repair in 33 cases. *J Vasc Surg* 2001; **33**: 106-13.
- 10) Knosalla C, Weng Y, Yankah AC, et al. Using aortic allograft material to treat mycotic aneurysms of the thoracic aorta. *Ann Thorac Surg* 1996; **61**: 1146-52.



» **Case Report** «

Traumatic Innominate Artery Pseudoaneurysm in the Setting of a Bovine Arch

Alfredo C. Cordova, MD,^{1,2} Frank W. Bowen, MD,^{2,3} Leigh A. Price, MD,¹
Stanley J. Dudrick, MD,⁴ and Bauer E. Sumpio, MD, PhD⁴

Blunt traumatic injury of the innominate artery occurs infrequently but is commonly lethal. Bovine aortic arch anatomy is a predisposition to this injury. Clinical findings, chest X-ray, and computerized tomography may suggest the diagnosis, and it may be confirmed with angiography. Both interposition and bypass grafting are operative repair methods of choice. EEG monitoring confirms cerebral perfusion, thereby allowing the deferment of shunts and cardiovascular bypass with hypothermic arrest. We report a case of traumatic innominate artery pseudoaneurysm in the setting of “bovine aortic arch” anatomy, together with multiple associated injuries, including descending aorta transection. We also review the current literature on the topic.

Key words: innominate artery, pseudoaneurysm, bovine arch, great vessel injury

INTRODUCTION

Innominate artery injury is an infrequent, but commonly fatal, occurrence. The majority of these injuries are caused by penetrating trauma, yet 35% are attributed to blunt trauma.^{1,2} It is estimated that 90% of patients die in the field or prior to arrival to the hospital.³ Nearly 100% of patients present with associated injuries, including rib fractures (46%), pneumothorax (36%), closed head injury, and liver and splenic lacerations.⁴

The most common aortic arch branching in humans consists of 3 great vessels originating from the aortic arch, including the innominate artery, the left subclavian artery, and the left common carotid artery (70% of the popula-

tion). The “bovine aortic arch” in humans is a misnomer and refers to an anatomical variant in which the left common carotid artery has a common origin with the innominate artery (13% prevalence; 25% blacks and 8% whites) or originates directly from the innominate artery (9% prevalence; 10% blacks and 5% whites). The “true bovine aortic arch” is present only in cattle and has no resemblance to any of the more than 20 different aortic arch configurations described in humans. In cattle, a single great vessel originates from the aortic arch and gives rise to both subclavian arteries and to a bicarotid trunk (**Fig. 1**).⁵ We report a case of a patient with a pseudoaneurysm of the innominate artery associated with multiple injuries, in the setting of a “bovine aortic arch,” secondary to blunt trauma.

CASE REPORT

A 32-year-old unhelmeted African American male was involved in a motor scooter accident. Chest Roentgenogram showed a widened mediastinum. Computed tomography of the chest suggested a great vessel injury (**Fig. 2**). Angiography revealed a “bovine aortic arch” and a pseudoaneurysm of the innominate artery (**Fig. 3**). In addition, he presented with a descending thoracic aorta transection at the level of the ligamentum arteriosum, right flail chest, bilateral hemo-pneumothoraces, grade 2 liver laceration, and multiple spinal fractures with no neurological deficits. The patient underwent innominate artery

¹Departments of Surgery, Johns Hopkins University School of Medicine, Baltimore, Maryland, USA

²Department of Surgery, Lahey Clinic Medical Center, Burlington, Massachusetts, USA

³Department of Cardiothoracic Surgery, Cooper University Hospital, Camden, New Jersey, USA

⁴Department of Surgery, Yale University School of Medicine, New Haven, Connecticut, USA

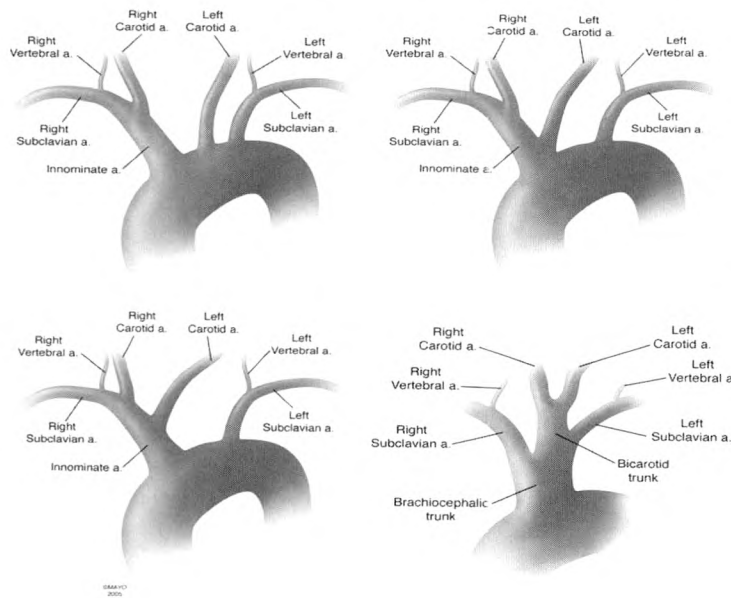
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Corresponding author: Alfredo C. Cordova, MD, Department of Surgery, Johns Hopkins University School of Medicine, 4940 Eastern Avenue, Baltimore, Maryland, USA

Tel: +1-410-550-6171, Fax: +1-410-550-8161

E-mail: acordova@jhu.edu

* Presented at the Southwestern Surgical Congress, Acapulco 2008.



A	B
C	D

Fig. 1 (A) "Normal aortic arch" anatomy, (B) "Bovine aortic arch," (C) "Bovine aortic arch," (D) true bovine arch. (Reproduced with permission of Layton, et al. and the American Journal of Neuroradiology⁵⁾)

* The figures are taken with permission from: Layton KF, Kallmes DF, Cloft HJ, Lindell EP, Cox VS. Bovine aortic arch variant in humans: clarification of a common misnomer. *AJNR Am J Neuroradiol.* 2006 Aug;27(7):1541-2. © American Society of Neuroradiology



Fig. 2 Computerized tomography showing 2.1 × 1.6 cm lesion suspicious for an innominate artery pseudoaneurysm. Significant subcutaneous emphysema evidenced on the upper chest wall bilaterally (arrows).



Fig. 3 Angiography demonstrating the bovine arch anatomy and a pseudoaneurysm (arrow) at the mid-portion of the innominate artery.

pseudoaneurysm repair with an interposition graft (DacronTM) from the ascending aorta (end-to-side anastomosis) to the right carotid-subclavian junction (end-to-end anastomosis) (**Fig. 4**). Heparin was administered by IV bolus prior to cross clamping the vascular structures. Intraoperative EEG monitoring was used continuously as an operative adjunct and confirmed adequate right cerebral hemispheric blood flow through the circle of Willis during 50 minutes of innominate artery cross clamping. Subsequently, a thoracic aortic stent graft (GoretxTM) was placed endovascularly to treat the descending aorta transection. Surveillance was undertaken to detect intra-abdominal bleeding in consideration of the presence of a liver laceration in the setting of intraoperative anticoagulation. Postoperatively, the patient developed deep vein thrombosis and ventilator-associated pneumonia, from which he recovered, and he was discharged ambulatory to home on the 30th post-operative day with no subsequent complications.

DISCUSSION

The innominate artery is the second most common site of blunt injury to the aortic arch vessels, the most common site being the aortic isthmus distal to the left subclavian artery.^{3,6)} It usually occurs at the origin of the innominate artery from the aortic arch,¹⁾ and can be caused by deceleration or crush injuries secondary to a motor vehicle crash or fall from a great height.^{3,6)} However, penetrating injuries more frequently cause innominate artery disruptions. Most patients die at the scene of the injury, but those who survive transportation to a medical facility are usually stable.

Karmy-Jones has reported the largest series of this injury.⁴⁾ In a retrospective study over a 5-year period, his team recognized 66 patients with aortic or great vessel injury, but only 8 patients presented with a blunt innominate artery disruption. He also reported that most of these injuries were proximal to the origin of the innominate

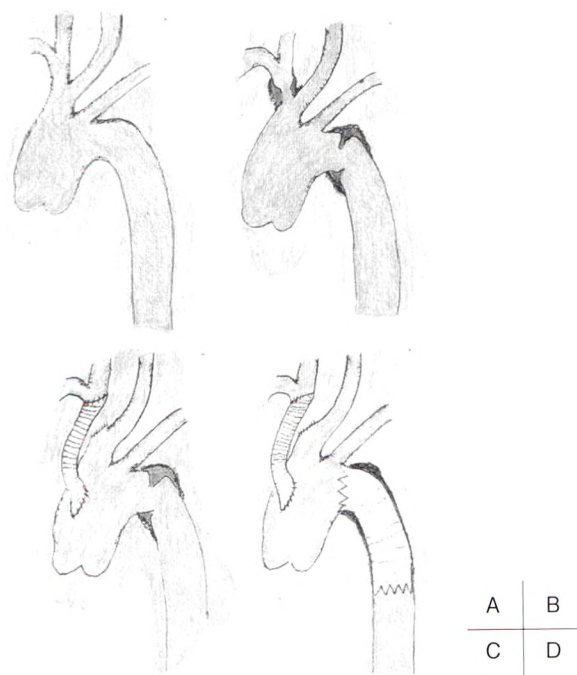


Fig. 4 (A) Bovine aortic arch anatomy. (B) Injuries at the level of the innominate artery and the descending aorta. (C) Interposition graft from the ascending aorta to the distal innominate artery just proximal to its bifurcation. (D) Endovascular graft of the descending aorta.

artery, and constituted 75% of his series. Depending on the location of the pseudoaneurysm, it was defined as proximal if $\leq$ than 0.5 cm from the origin, distal if $\leq$ than 0.5 cm from the innominate artery bifurcation, and middle if between the proximal and distal locations.⁴⁾ The prevalence of bovine arch anatomy is 22% and is more common in the black population. It is believed that this anatomic variant carries with it a relative predisposition for sustaining blunt injury at the innominate artery due to the decreased number of fixation points on the aortic arch. Secondary to blunt trauma, the innominate artery is compressed between the sternum and the spine, and the resulting shear forces cause a tear or transection.^{2, 7)} This anteroposterior compression of the mediastinum between the sternum and the vertebrae displaces the heart posteriorly and to the left, increasing the curvature of the arch and causing tension on the outlet vessels. In addition, hyperextension of the cervical spine and left lateral head rotation places traction on the right carotid artery, which imposes further tension on the innominate artery.¹⁾ In our patient, shearing of the artery by posterior displacement of the manubrium was the cause of the injury. Injuries to this common trunk jeopardize the vascular integrity of both carotid arteries and the right vertebral artery.³⁾

Clinically, this injury may be associated with supraclavicular hematoma, bruit, pulse deficit, and a shoulder-belt sign (ecchymosis from the base of the right neck to the chest).⁴⁾ Screening chest X-rays and computerized tomography may suggest the presence of this injury, which is confirmed by angiography, the gold standard study.⁸⁾ Chest X-ray usually shows widening of the superior mediastinum, particularly on the right side. Standard computerized tomography is insufficient to confirm or rule out this injury, as visualization of the aortic arch anatomy is not reliable. CT angiogram with 3-D reconstructions may supply sufficient information to establish the diagnosis and permit operation, however, if it is non-conclusive, angiography might still be required. Chu, et al., reported a case of associated aortic valve rupture and proposed that all patients with blunt innominate artery injury should undergo a transesophageal echocardiography to evaluate the integrity of the aortic valve and to aid in the assessment of ascending and descending aorta.⁶⁾

Surgical exposure is achieved by the use of a median sternotomy,^{3, 8)} which effectively allows control of hemorrhage and repair of the injury. With this approach, injuries to the ascending aorta, innominate artery, and left common carotid artery can be exposed. For injuries to the left subclavian artery or the descending aorta, a left thoracotomy is necessary.³⁾ Interposition or bypass graft, with or without shunts; cardiopulmonary bypass with hypothermic arrest; and combined endovascular and open repairs have been proposed as approaches to treating this injury. In this case, interposition graft was considered ideal, and was performed without shunting because the information obtained by continuous intraoperative EEG monitoring confirmed adequate cerebral blood supply after cross clamping the vasculature. This injury was surgically managed by performing a proximal side-to-end anastomosis of the graft to the ascending aorta and a distal end-to-end anastomosis of the graft to the innominate artery, followed by closure of the aneurysmal lesion. Cardiopulmonary bypass has been used for repair of these injuries and is usually performed in the absence of concomitant neurological injury. However, it is required only if there is evidence of heart failure.⁴⁾ Hypothermic circulatory arrest may also be necessary in patients with extensive aortic calcification. Endovascular approaches have also been reported.⁹⁾ In our case, an endovascular approach was not possible because an adequate distal innominate artery "landing zone" was not available. Distal injuries may require the use of Y-grafts. Resection of the aneurysm and primary anastomosis have been proposed for lesions

not associated with extensive tissue loss or tension.⁴⁾ Retrograde cerebral perfusion has been associated with post-operative neurological dysfunction, however, some authors dispute this. It also extends operating time and may cool the brain down an additional 10°C.²⁾

Cerebral perfusion is maintained through retrograde flow from the subclavian and vertebral arteries after placing the vascular clamps proximal to the subclavian-carotid artery bifurcation.⁸⁾ Angiogram may confirm adequate collateral supply via the Circle of Willis. Also, back bleeding and stump pressure may demonstrate retrograde blood flow from the contralateral vertebral artery.⁴⁾ During the vascular repair in our patient, cerebral circulation was reassured through the use of EEG monitoring, whereby we traced 4 leads of each hemisphere. While bilateral symmetry and amplitude of the EEG confirms adequate cerebral perfusion, a decreased amplitude or electrical silence indicates inadequate flow and triggers the neurophysiologist to alert the surgeon to secure cerebral perfusion. In our case, encephalic electric wave symmetry was observed throughout the case, and neither cardiopulmonary bypass nor shunting was necessary.

Risk of systemic anticoagulation in the presence of known liver laceration demanded aggressive surveillance. Although anticoagulation carries an increased risk of associated intra-abdominal or orthopedic bleeding, it usually does not manifest itself if diagnosed and managed appropriately prior to the vascular procedure.¹⁾

Studies have shown that preoperative central nervous system deficits are associated with higher mortality.¹⁾ In the presence of cerebral injury, surgery is usually delayed, and endovascular repairs should be considered. This should also apply to those patients with significant comorbidities that preclude major surgical interventions. A relatively central innominate artery injury is required in order to secure adequate "landing zones" for the endovascular prosthesis proximally and distally. It has been proposed that endovascular grafts are best deployed via the right common carotid artery, thus allowing a direct approach to the brachiocephalic artery.⁴⁾ Johnston, et al., reported a 30 year experience in which associated injuries increased the mortality from 8 to 30%.¹⁰⁾ Most series advocate prompt or immediate repair; however, some have demonstrated the feasibility of delayed repair.¹¹⁾

CONCLUSION

In a trauma setting, the presence of bovine arch anatomy predisposes patients to great vessel injury and com-

plicates repair. Chest X-ray, computerized tomography, CT angiography may suggest the diagnosis, but angiography is the preferred confirmatory test. Interposition graft from the ascending aorta to the distal innominate artery constitutes the treatment of choice. Intraoperative continuous EEG monitoring is a useful adjunct, as it can provide vital information regarding cerebral blood flow, and may simplify reconstruction by avoidance of more complex shunting, or circulatory arrest with retrograde cerebral perfusion. Despite the low frequency and high lethality of this injury, early recognition and prompt repair usually yield good results. Because of the high risk of rupture of an injured innominate artery, especially in the setting of a "bovine aortic arch," urgent definitive diagnosis and judicious operative management are mandatory for achieving optimal outcomes.

REFERENCES

- 1) Veerasingham D, Vioreanu M, O'Donohue M, et al. Traumatic transection of the innominate artery. *Interact Cardiovasc Thorac Surg* 2003; **2**: 569-71.
- 2) Moise MA, Hsu V, Braslow B, et al. Innominate artery transection in the setting of a bovine arch. *J Thorac Cardiovasc Surg* 2004; **128**: 632-4.
- 3) Al-Khalidi A, Robbins RC. Successful repair of blunt injury of aortic arch branches in the setting of bovine arch. *J Vasc Surg* 2006; **43**: 396-8.
- 4) Karmy-Jones R, DuBose R, King S. Traumatic rupture of the innominate artery. *Eur J Cardiothorac Surg* 2003; **23**: 782-7.
- 5) Layton KF, Kallmes DF, Cloft HJ, et al. Bovine aortic arch variant in humans: clarification of a common misnomer. *AJNR Am J Neuroradiol* 2006; **27**: 1541-2.
- 6) Chu MW, Myers ML. Traumatic innominate artery disruption and aortic valve rupture. *Ann Thorac Surg* 2006; **82**: 1095-7.
- 7) Wells P, Estrera A. Blunt traumatic innominate pseudoaneurysm and left common carotid occlusion with an associated bovine aortic arch. *J Thorac Cardiovasc Surg* 2005; **130**: 928-9.
- 8) Cothren CC, Moore EE. Posttraumatic innominate artery pseudoaneurysm. *J Am Coll Surg* 2005; **201**: 806-7.
- 9) Zoffoli G, Saccani S, Larini P, et al. Endovascular treatment of traumatic aortic dissection and innominate artery pseudoaneurysm. *J Trauma* 2006; **61**: 447-50.
- 10) Johnston RH Jr, Wall MJ Jr, Mattox KL. Innominate artery trauma: a thirty-year experience. *J Vasc Surg* 1993; **17**: 134-40.
- 11) Mauney MM, Cassada DC, Kaza AK, et al. Management of innominate artery injury in the setting of bovine arch anomaly. *Ann Thorac Surg* 2001; **72**: 2134-6.

» **Case Report** «

Focal Renal Arterial Fibromuscular Dysplasia Demonstrated via Intravascular Ultrasound Image

Osamu Ogawa, MD, Ritsuo Watanabe, MD, Hiroshi Shimizu, MD, and Fumiaki Masani, MD

A young male suffering from renovascular hypertension was admitted. His initial arteriogram highlighted a focal stenosis of the right renal artery. His intravascular ultrasound (IVUS) revealed increasing medial layer thickness accompanied by a mixture of both high and low echoic materials in this layer. There was also mild thickening of the intimal layer. The diagnosis of medial fibroplasia and intimal fibromuscular dysplasia (FMD) was made. Balloon angioplasty decreased the volume of dysplastic tissue. The IVUS images facilitated both the initial diagnosis of focal renal arterial stenosis and the evaluation of the mechanism of dilatation by angioplasty.

Key words: fibromuscular dysplasia, intravascular ultrasound, percutaneous renal angioplasty

INTRODUCTION

Fibromuscular dysplasia (FMD) is a group of both non-atherosclerotic and non-inflammatory vascular diseases.^{1–2)} Although the strict diagnosis of FMD should be decided via histopathological examination, the gold standard for diagnosing FMD is an arterial angiogram. The characteristic “string-of-beads” feature is found in the majority of such patients. In focal and tubular FMD stenosis cases, a differential diagnosis also needs to be performed. Such arterial diseases include both atherosclerotic and/or inflammatory types. IVUS is a useful tool, in addition to the angiography for evaluation of both the anatomical changes of structures of the vessel layer and observation of tissue characteristics. Currently, it is understood that publications related to IVUS images of focal or tubular types of FMD are limited. This report therefore presents IVUS images of focal type FMD.

Division of Cardiology, Niigata Prefectural Central Hospital, Joetsu, Niigata, Japan

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Corresponding author: Osamu Ogawa, MD. Division of Cardiology, Niigata Prefectural Central Hospital, Shinnann-cyo 205, Joetsu, Niigata 943-0192, Japan
Tel: +81-25-522-7711, Fax: +81-25-521-3720
E-mail: oogawa@npch.lamen.or.jp

CASE REPORT

A 20-year-old man with resistant hypertension was admitted. He suffered from occasional headaches over a period of two years. His blood pressure was approximately 180/110 mmHg, despite consistently following his prescription of calcium channel blockers over a period of six months. Although the previous medical history was sound, his grandparents had suffered as well from hypertension. A closer inspection of secondary hypertension was carried out. Urinalysis showed proteinuria, while the blood chemistry demonstrated normal renal function. However, both plasma aldosterone concentration (PAC) and plasma rennin activity (PRA) were elevated (PAC was 39.2 ng/dL, PRA was 37.39 ng/mL/hr). In the abdominal duplex scanning, peak systolic velocity of the right renal artery and renal aortic ratio of his right kidney were high (303 cm/s and 2.0 respectively). Enhanced abdominal computed tomography revealed a severe focal stenosis in the mid portion of his right renal artery. Renal arterial stenosis with both hyperreninemia and hyperaldosteronemia indicated the diagnosis of renovascular hypertension. Since this patient was a young adult with no other atherosclerotic risk factors, and since the arterial lesion existed in the mid portion of the renal artery, it was suggested to be caused by a non-atherosclerotic mechanism.

The renal angiography showed focal severe stenosis in the mid portion of his right renal artery (**Fig. 1A**).

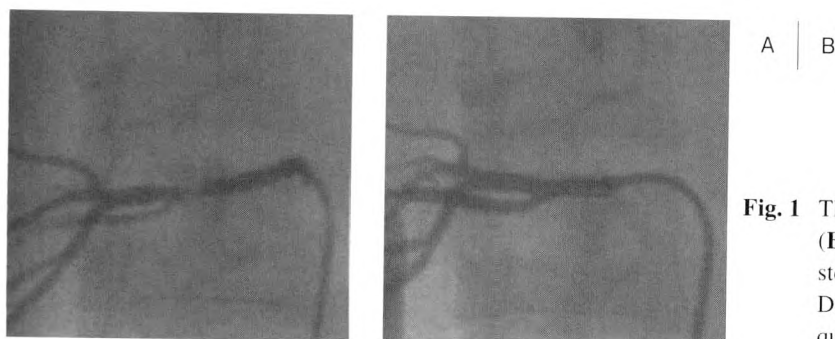


Fig. 1 The right renal arteriographies before (A) and after (B) angioplasty. The left panel shows discrete focal stenosis in the mid portion of the right renal artery. Diameter stenosis decreased from 74 % to 14 % as quantitatively measured in angiographies.

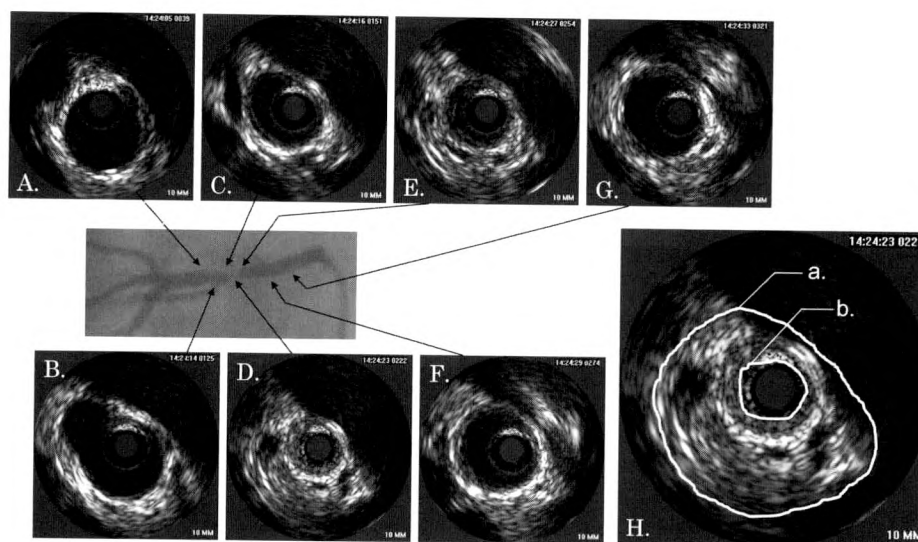


Fig. 2 Intravascular ultrasound (IVUS) images along inside of the right renal artery. Alphabetical order of the images as arranged in the positional order of the artery. Example, A, is the most distal site and G, is the most proximal site of the artery. H, is a magnified image of the lesion (D): a, is the outer line of media and b, is the endoluminal line of the artery.

A percutaneous renal angioplasty of this lesion was performed. A single 20-MHz transducer (Eagle Eye, 2.9 Fr., Volcano, Fukuda Denshi Co) using auto-pullback system (0.5 mm/s) was employed to observe this lesion before and after angioplasty. Before angioplasty, the reference vessel diameter (measured between external elastic membranes) was about 4.8 mm and the minimal luminal diameter at the lesion was approximately 2.1 mm. The length of lesion was approximately 9.8 mm. Neither arterial stenosis nor arterial wall abnormalities were observed other than in this lesion (**Fig. 2**). Initially, the renal artery appeared to be negatively remodeling around the lesion. The cross-sectional area surrounded by internal high echoic lines appeared to diminish (the vessel appeared to be shrunk). Following further observation, eccentric medial thickening between internal high echoic line and outer high echoic line was coexisting with mild intimal thickening (from 4 o'clock to 11 o'clock in cross-sectional view of the

IVUS image in **Fig. 2D** and **2H**). Furthermore, mottled mixtures of high and low echoic material in this thickening medial layer were recognized. An eccentric ridge due to medial thickening with mild intimal thickening caused narrowing of the vessel (**Fig. 2H**, **Fig. 3A** and **3C**). These findings were clearly different from that of an atherosclerotic lesion. The high echoic materials in this thickened media perhaps signified elastin and collagen deposition in this layer. This, in turn, might be compatible with medial FMD. Intimal and subintimal layers also mildly thickened and appeared highly echogenic. A final diagnosis of the renal arterial lesion as a medial fibroplasia coexistent with mild intimal FMD was made.

A balloon angioplasty (balloon diameter of 4.5 mm) on this lesion was performed, which resulted in successful dilatation of stenosis without stent implantation (**Fig 1B**). After angioplasty, the IVUS images showed a decrease in thickness of eccentric ridges of the medial layer (from 2.6

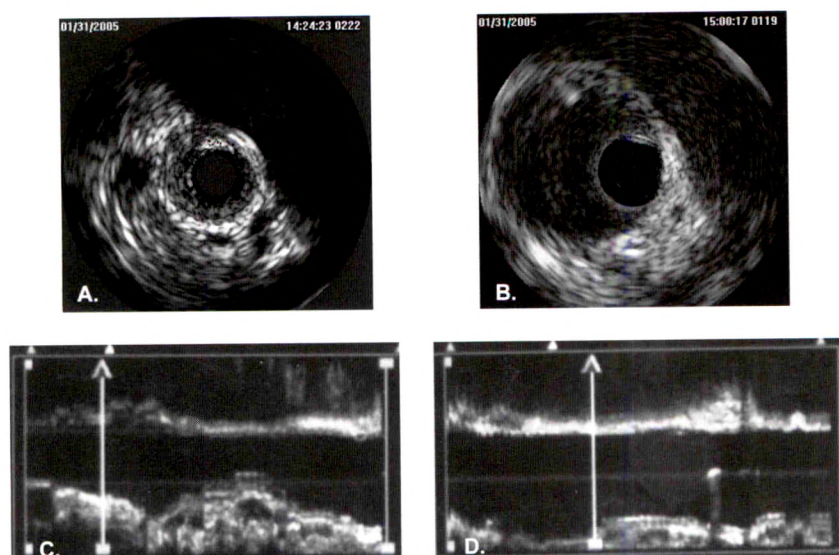


Fig. 3 Upper panels: The IVUS images at the minimal luminal lesion before (A) and after (B) angioplasty. Lower panels: The reconstructed longitudinal IVUS image around the lesion of the right renal artery before (C) and after (D) angioplasty.

mm to 1.3 mm), while a thickness of intimal layer (which was thickening mildly) also decreased (from 0.9 mm to 0.5 mm). There was a residual thickening layer from 3 o'clock to 7 o'clock in cross-sectional view of the IVUS image in **Fig. 3B**. The vessel diameter showed little change. In sum, a significant reduction in volume of the dysplastic tissue occurred through the balloon angioplasty. Following angioplasty, the minimal luminal diameter at the lesion increased to 4.4 mm. Area stenosis decreased from 84.2 % to 22.6 % (**Fig. 3**). Such findings suggested that the primary mechanism of dilatation of this focal FMD lesion could have been crashing and/or cracking of thick and dysplastic layers. This also suggested that diseased layers with fibroplasia might be softer than expected.

Following angioplasty, the patient's blood pressure gradually returned to normality (approximately 120/80 mmHg) without the use of antihypertensives. His renal function remained to be normal. Seven months later, a peak systolic velocity of the right renal artery was 107 cm/s, and the right renal aortic ratio was 0.8 in abdominal duplex scanning.

DISCUSSION

FMD is a group of dysplastic changes of one or more layers of medium-sized or large arteries.¹⁻²⁾ FMD most commonly affects the renal and internal carotid arteries. Although the disease consists of a heterogeneous group of histologic changes, FMD lesions show dysplastic changes (pure hyperplasia in rare cases) of fibrous, smooth muscles or fibromuscular tissue. In such cases,

there is neither lipid deposition nor inflammatory cell infiltration. FMD occurs predominantly in young to middle-aged female individuals with a predilection for disease in the right renal artery. Although a variety of genetic, mechanical and hormonal factors have been proposed, the actual cause of FMD remains unknown.

A pathological classification of renal artery FMD was proposed by McCormack et al.³⁻⁴⁾ It was based on the dominant arterial wall layer involved: the intima, media or adventitia. Intimal FMD, which accounts for 5 % of renal artery FMD cases, is characterized by irregularly arranged mesenchymal cells within a loose matrix of sub-endothelial connective tissue and a fragmented internal elastic lamina. Medial FMD accounts for up to 95 % of cases, and has been further subdivided into medial fibroplasia, perimedial fibroplasia, and medial hyperplasia.⁵⁾ Perimedial fibroplasia implies a predominance of fibrous tissue, and the proliferation is primarily at the junction of the media and adventitia. Pure medial hypertrophy is rare and represents a concentric hypertrophy of the medial wall. This is relatively smooth, lacking fibrosis, and causes severe stenosis. In adventitial fibroplasia (the rarest type of FMD), the primary lesion is a dense collagenous replacement of the loose fibrous tissues of the arterial adventitia. The above types are not mutually exclusive; indeed, medial and perimedial FMD lesions can coexist in the same arterial segment. Furthermore, more than one arterial layer can be involved in the same patient.⁵⁾

The lesions in some types of FMD are of a homogeneous appearance of elastic tissue that presents itself as a multiple stenosis interspersed with aneurismal outpouchings. Such pathologic changes are demonstrated by a

"string-of-beads" appearance via angiography.⁴⁻⁶⁾ The "string-of-beads" appearance, which angiographically characterized medial FMD, occurs in about 70 % of cases. Specific features of adventitial or intimal FMD cannot be shown using angiography.⁴⁻⁷⁾ Focal or tubular angiographic aspects cannot be related to specific histological lesions. In cases with focal and tubular FMD stenosis, differential diagnoses are atherosclerotic or inflammatory arterial disease, vascular Ehlers-Danlos and Williams' syndromes, and type 1 neurofibromatosis, etc.²⁾ FMD lesions are typically truncal or distal, as opposed to atherosclerotic stenosis, which are mostly ostial or proximal.

Ultrasonography relies on differences in both tissue reflectivity and sound penetration to determine tissue composition. Smooth muscle or lipid-containing plaques are hypo-echoic, whereas fibrous tissue, collagen, elastin, or calcified plaque are hyper-echoic. In this manner, current ultrasound imaging provides the capability for an in-vivo pathologic examination. IVUS is a method for detecting a diseased arterial wall anatomy which can be underestimated or even completely inapparent from angiography. Furthermore, IVUS can identify all three layers of an artery and also detect the mostly involved layer of a diseased artery. The published reports about relation of IVUS images with histopathological findings of renal FMD are presently limited. Although several reports show the relation of IVUS image with the "string-of-beads" type FMD, there are few reports about focal renal FMD.⁸⁻¹⁰⁾ Furthermore, most of publications make little mention of the pathological evaluation of the lesions and describe only both the evaluation of the lesion form (size) and how to use the IVUS as a decision maker of interventional strategy.

In this present case, IVUS revealed which layer was involved, what ultrasound findings appeared in each layer, and how the diseased layer changed by angioplasty. The appearance of mottled high echoic materials in the medial layer may indicate existence of fibrous tissue, collagen and elastin in this layer and disorganization of this tissue, as well. Although this lesion represented as a focal stenosis on the angiography, it instead was medial fibroplasia, possibly with mild intimal fibroplasia. The medial fibroplasia is a major type of FMD, and 60%-70% of this type show "string-of-beads" appearance via angiography.⁴⁻⁷⁾ IVUS was useful in differentiation of FMD from atherosclerosis in such a focal stenosis type via angiography. Furthermore, IVUS images were useful in not only the evaluation of both the lesion diameter and lesion form, but also decision making of both balloon size and end point of strategy. In this case, IVUS images also suggested a

mechanism of dilatation of this FMD lesion.

Although IVUS can't give full information about histopathological change, it is able to indicate which layer is predominantly involved in the lesion. Furthermore, it also suggests tissue characteristics according to echogenic types, as well. Such information enables comprehensive understanding for a correct diagnosis.

In conclusion, the potential value of IVUS imaging is investigated as a way to overcome the limitations of angiography in characterizing the renal artery structure. IVUS imaging is feasible and can be conducted without significantly prolonging the procedure time or increasing the risk of complications.

DISCLOSURE STATEMENT

No grants were utilized for this report.

The authors state that they have no Conflict of Interest (COI).

REFERENCES

- 1) Slovut DP, Olin JW. Fibromuscular dysplasia. *N Engl J Med* 2004; **350**: 1862-71.
- 2) Plouin PF, Perdu J, Batide-Alanore AL, et al. Fibromuscular dysplasia. *Orphanet J of Rare Dis* 2007; **2**: 28-35.
- 3) Harrison EG, McCormack LJ. Pathologic classification of renal arterial disease in renovascular hypertension. *Mayo Clin Proc* 1971; **46**: 161-7.
- 4) McCormack LJ, Poutasse EF, Meaney TF, et al. A pathologic-arteriographic correlation of renal arterial disease. *Am Heart J* 1966; **72**: 188-98.
- 5) Alimi Y, Mercier C, Pellissier JF, et al. Fibromuscular disease of the renal artery: A new histopathologic classification. *Ann Vasc Surg* 1992; **6**: 220-4.
- 6) Kimura K, Ohtake H, Kato H, et al. Multivisceral fibromuscular dysplasia: an unusual case of renal and superior mesenteric involvement. *Ann Vasc Dis* 2010; **3**: 152-6.
- 7) Kincaid OW, Davis GD, Hallermann FJ, et al. Fibromuscular dysplasia of the renal arteries: arteriographic features, classification, and observation on natural history of the disease. *Am J Roentgenol* 1968; **104**: 271-82.
- 8) Sheikh KH, Davidson CJ, Newman GE, et al. Intravascular ultrasound assessment of the renal artery. *Ann Intern Med* 1991; **115**: 22-5.
- 9) Gowda MS, Loeb AL, Crouse LJ, et al. Complementary roles of color-flow duplex imaging and intravascular ultrasound in the diagnosis of renal artery fibromuscular dysplasia. *J Am Coll Cardiol* 2003; **41**: 1305-11.
- 10) Prasad A, Zafar N, Mahmud E. Assessment of renal artery fibromuscular dysplasia: angiography, intravascular ultrasound (with virtual histology), and pressure wire measurements. *Catheter Cardiovasc Interv* 2009; **74**: 260-4.

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- (1) 出血している患者(血友病、毛細血管脆弱症、上部消化管出血、尿路出血、喀血、眼底出血等)
- (2) 妊婦又は妊娠している可能性のある婦人

【効能・効果】

- 慢性動脈閉塞症に伴う潰瘍、疼痛及び冷感の改善
- 原発性肺高血圧症

<効能・効果に関連する使用上の注意> 原発性肺高血圧症

- (1) 原発性肺高血圧症と診断された患者にのみ使用すること。
- (2) 本剤は経口投与であるため、重症度の高い患者等では効果が得られにくい場合がある。循環動態あるいは臨床症状の改善が見られない場合は、注射剤や他の治療に切り替えるなど適切な処置を行うこと。

【用法・用量】

- 慢性動脈閉塞症に伴う潰瘍、疼痛及び冷感の改善 通常、成人には、ペラプロストナトリウムとして1日120 μ gを3回に分けて食後に経口投与する。
- 原発性肺高血圧症 通常、成人には、ペラプロストナトリウムとして1日60 μ gを3回に分けて食後に経口投与することから開始し、症状(副作用)を十分観察しながら漸次増量する。増量する場合、投与回数を1日3~4回とし、最高用量を1日180 μ gとする。

<用法・用量に関連する使用上の注意> 原発性肺高血圧症

原発性肺高血圧症は薬物療法に対する忍容性が患者によって異なることが知られており、本剤の投与にあたっては、投与を少量より開始し、増量する場合は患者の状態を十分に観察しながら行うこと。

【使用上の注意】(抜粋)

1. 慎重投与(次の患者には慎重に投与すること) (1) 抗凝血剤、抗血小板剤、血栓溶解剤を投与中の患者(「相互作用」の項参照) (2) 月経期間中の患者[出血傾向を助長するおそれがある。] (3) 出血傾向並びにその素因のある患者[出血傾向を助長するおそれがある。]
2. 重要な基本的注意 (1) 本剤の有効成分は「ケアロードLA錠60 μ g」、「ペラサスLA錠60 μ g」と同一であるが、原発性肺高血圧症において用法・用量が異なることに注意すること。(2) 原発性肺高血圧症において「ケアロードLA錠60 μ g」、「ペラサスLA錠60 μ g」から本剤へ切り替える場合には、「ケアロードLA錠60 μ g」、「ペラサスLA錠60 μ g」の最終投与時から12時間以上が経過した後に、本剤をペラプロストナトリウムとして原則1日60 μ gを3回に分けて食後に経口投与することから開始すること。また、「ケアロードLA錠60 μ g」、「ペラサスLA錠60 μ g」と同用量の本剤に切り替えると、過量投与になるおそれがあるため注意すること。
3. 相互作用 併用注意(併用に注意すること) 抗凝血剤(ワルファリン等)、抗血小板剤(アスピリン、チクロピジン等)、血栓溶解剤(ウロキナーゼ等)、プロスタグランジン₁₂製剤(エボprostステノール、ペラプロスト[®]11)、エンドセリン受容体拮抗剤(ボセンタン) 注1) 同一有効成分を含有する「ケアロードLA錠60 μ g」、「ペラサスLA錠60 μ g」等との併用に注意すること。
4. 副作用 ○慢性動脈閉塞症に伴う潰瘍、疼痛及び冷感の改善 総症例7,515

例中、370例(4.9%)に副作用(臨床検査値異常を含む)が認められ、その主なものは頭痛91例(1.2%)、顔面潮紅60例(0.8%)、ほてり39例(0.5%)、下痢29例(0.4%)、嘔気20例(0.3%)等であった。

○再審査結果通知:1999年3月
○原発性肺高血圧症 肺高血圧症の臨床試験において総症例40例中、24例(60.0%)に副作用(臨床検査値異常を含む)が認められ、その主なものは頭痛9例(22.5%)、LDH上昇5例(12.5%)、ビリルビン上昇4例(10.0%)、ほてり3例(7.5%)、下痢3例(7.5%)、嘔気3例(7.5%)、トリグリセライド上昇3例(7.5%)等であった。

(効能追加時:1999年9月)
使用成績調査において総症例244例中、57例(23.4%)に副作用(臨床検査値異常を含む)が認められ、その主なものは頭痛15例(6.1%)、AST(GOT)上昇9例(3.7%)、ALT(GPT)上昇8例(3.3%)、ほてり8例(3.3%)、顔面潮紅4例(1.6%)、倦怠感4例(1.6%)等であった。このうち、小児(15歳未満)については66例中、14例(21.2%)に副作用(臨床検査値異常を含む)が認められ、その主なものは鼻出血3例(4.5%)、AST(GOT)上昇3例(4.5%)、ALT(GPT)上昇3例(4.5%)、頭痛2例(3.0%)、ほてり2例(3.0%)等であった。(再審査申請時)
(1) 重大な副作用 1) 出血傾向[脳出血(0.1%未満)、消化管出血(0.1%未満)、肺出血(0.1%未満)、眼底出血(0.1%未満)]:観察を十分に行い、異常が認められた場合には投与を中止し、適切な処置を行うこと。2) ショック(0.1%未満)、失神(0.1%未満)、意識消失(0.1%未満):ショック、失神、意識消失を起こすことがあるので、観察を十分に行い、血圧低下、頻脈、顔面蒼白、嘔気等が認められた場合には投与を中止し、適切な処置を行うこと。3) 間質性肺炎(頻度不明^{※2}):間質性肺炎があらわれることがあるので、観察を十分に行い、異常が認められた場合には投与を中止し、適切な処置を行うこと。4) 肝機能障害(0.1%未満):黄疸や著しいAST(GOT)、ALT(GPT)の上昇を伴う肝機能障害があらわれることがあるので、観察を十分に行い、このような場合には投与を中止し、適切な処置を行うこと。5) 狭心症(頻度不明^{※2}):狭心症があらわれることがあるので、異常が認められた場合には投与を中止し、適切な処置を行うこと。6) 心筋梗塞(頻度不明^{※2}):心筋梗塞があらわれるとの報告があるので、異常が認められた場合には投与を中止し、適切な処置を行うこと。注2) 自発報告によるものについては頻度不明。

【承認条件】

原発性肺高血圧症において可能な限り、再審査期間中の全投与症例を使用成績調査の対象とすること。なお、予後に関する成績も収集すること。

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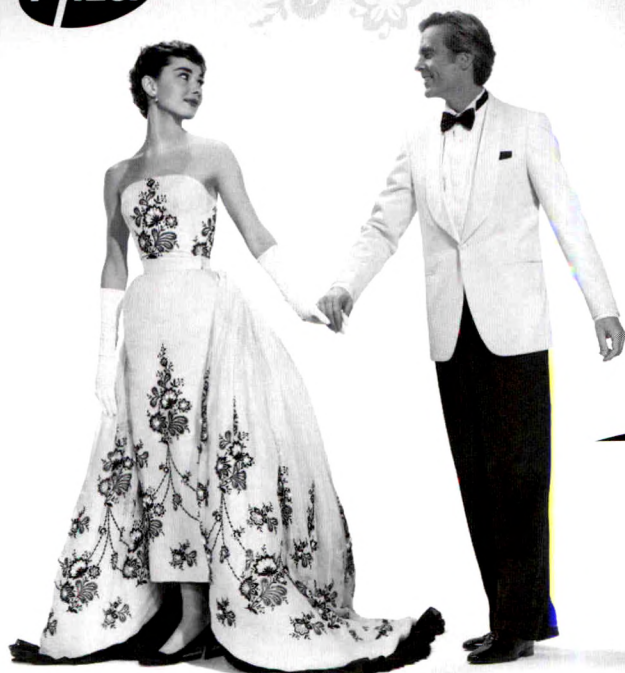
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The Annals of Vascular Diseases is an emerging journal launched from Japan in 2007.

The Journal publishes peer-reviewed original articles, editorials, reviews, case reports and others in vascular research, vascular medicine, surgery, and the allied fields. Several journals dedicated to the vascular field exist in Asia including Japan. The **Japanese College of Angiology**, the **Japanese Society for Vascular Surgery** and the **Japanese Society of Phlebology**, therefore, collaborated to sponsor this new journal to jump-start the development and maturity of this growing field. Since October 2008 and June 2010, AVD has been the Official Journal of **Asian Society for Vascular Surgery** and **Asian Venous Forum** as well respectively.

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Magnetic Resonance Angiography of the Aorta

Yasuo Takehara, MD, DMSc,¹ Shuhei Yamashita, MD, PhD,² Harumi Sakahara, MD, PhD,²
Takayuki Masui, MD, PhD,³ and Haruo Isoda, MD, PhD⁴

Magnetic resonance angiography (MRA) is capable of imaging arteries in the half to whole body by a single acquisition without a nephrotoxic contrast medium, and acquired images can be reconstructed into a specific cross-sectional view in an arbitrary directions. MRA is applicable for vessels non-reachable by a catheter approach, and collateral vessels can be fully visualized. Since MRA is minimally-invasive with no exposure to ionized radiation, it can be repeatedly applied for follow-up. However, there are also disadvantages: the temporal and spatial resolutions are inferior to those of X-ray angiography, and, at present, it cannot be used as a guide for intervention. Moreover, gadolinium administrations may cause NSF in patients who have lost renal function, as a new risk. Accordingly, strict consideration is required for an indication of its application. Development of non-contrast MRA and evaluation of the wall itself may draw more attention in the future. Plaque imaging is being routinely performed nowadays, and the measurement of vascular wall shear stress, which has a close association with arteriosclerosis, may become possible by utilizing the time-resolved phase-contrast method capable of measuring the time-resolved velocity vectors of blood flow throughout the body. (*English Translation of J Jpn Coll Angiol, 2009, 49: 503-516.)

Keywords: contrast-enhanced MRA, non-contrast MRA, flow analysis, atherosclerosis

ADVANTAGES OF MR ANGIOGRAPHY

The current modalities to evaluate aortic pathologies include digital subtraction angiography (X-ray DSA), X-ray CT, Doppler ultrasonography (US), and intra-vascular ultrasonography (IVUS). Of these, magnetic

resonance angiography (MRA) is recommended for the following reasons:

1) MRA is a modality without nephrotoxicity

Generally, patients requiring imaging of the aorta have underlying diseases likely to lead to renal dysfunction, such as diabetes and arteriosclerosis, for which the risk of X-ray angiography using iodinated contrast media. X-ray contrast media employs iodinated contrast media, which have been reported to be one of the major factors of hospital-acquired renal insufficiency.¹⁾ Many patients indicated for lower limb X-ray angiography are complicated by diabetes and renal stenosis due to arteriosclerosis and have renal dysfunction, and the risk of iodinated contrast medium-induced renal failure is greater than that in patients with other diseases.

The nephrotoxicity of gadolinium contrast medium is very low,²⁾ and moreover, non-contrast imaging may also be selected if necessary, although the image quality may not be satisfactory. MRA and US are the only imaging

¹Radiology, Hamamatsu University Hospital, Hamamatsu, Shizuoka, Japan

²Radiology, Hamamatsu University School of Medicine, Hamamatsu, Shizuoka, Japan

³Radiology, Seirei Hamamatsu General Hospital, Hamamatsu, Shizuoka, Japan

⁴Radiological Technology, Nagoya University School of Health Sciences, Nagoya, Aichi, Japan

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Corresponding author: Yasuo Takehara, MD, DMSc. Radiology, Hamamatsu University Hospital, 1-20-1 Handayama, Higashi-ku, Hamamatsu, Shizuoka 431-3192, Japan

Tel: +81-53-435-2242, Fax: +81-53-435-2241

E-mail: takehara@hama-med.ac.jp

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methods applicable for vascular evaluation without a concern for renal function in patients at risk of a declining renal function. MRA is superior for maintaining the renal function among contrast imaging methods.

After the non-nephrotoxicity of gadolinium became widely known, X-ray DSA with the arterial administration of a large amount of gadolinium chelates had been attempted. It has been reported that intravenously administered gadolinium is mostly non-nephrotoxic, but, considering its high osmolality, it has been controversial whether it is completely non-nephrotoxic when intra-arterially administered.³⁾

Nephrogenic systemic fibrosis (NSF) is the additional concern when a large amount of contrast medium is administered for X-ray DSA or MRA, because a dose-dependent risk is known for NSF.⁴⁾

2) No requirement of catheter approach to the target artery

MRA is capable of imaging blood vessels in any region of the body even in patients with bilateral femoral arterial obstructions and bilateral brachial and axillary arterial obstructions for which the Seldinger's technique is not applicable. Translumbar aortography with direct puncture of the abdominal aorta (Dos Santos method), which is very invasive and high-risk, was previously applied for patients with obstructions of the femoral, brachial, and axillary arteries in which the Seldinger technique was non-applicable.

3) Three-dimensional data collection by a single acquisition (possible to observe an arbitrary section)

Since MRA is capable of 3-dimensional display, observation from various directions is possible on single contrast medium injection. To acquire images in various directions on X-ray angiography, contrast medium has to be injected each time (imaging of each region is necessary when imaging with table-moving acquisition is not possible), which is unfavorable because it affects renal function but also leads to an extra cost.

4) Collateral vessels are not missed

Since contrast-enhanced MRA is performed through transvenous contrast administration, all collateral vessels and bypasses can be depicted (Fig. 1). In the catheter method, only downstream blood vessels from the injected



Fig. 1 Three-dimensional contrast-enhanced MRA of a middle-aged woman with coarctation of the aorta. There is a short segment of stenosis at the proximal portion of the thoracic descending aorta (→) after it branches to the left subclavian artery. Note numerous collaterals that developed in the thoracic wall are well depicted in this contrast-enhanced MRA, which cannot be entirely delineated by a single catheter technique.
MRA: magnetic resonance angiography

site are imaged. For example, in patients with obstruction of the abdominal aorta through the common iliac artery, collateral vessels through the thoracic wall (internal mammary artery) and abdominal walls (inferior epigastric artery) are important, but individual imaging of all these vessels employing the catheter method requires approaches to many blood vessels, which is very complex and requires repeated catheter approaches, contrast medium administration, and exposure to ionized radiation.

5) Simple post-processing

In MRA, high-intensity regions are mostly limited to vascular lumens, which can be easily processed after acquisition. This is a marked advantage of image reconstruction compared to CT, which requires the removal of high density structures, such as bone and severe calcification of vascular walls.

6) Appropriate for follow-up after interventional treatment

Generally, vascular imaging is repeated after treatment to evaluate and follow the effect of various interventions (surgical, radiological, and pharmacological interventions), but repeated angiography employing the invasive catheter method is unfavorable regarding the QOL of patients as well as medico-economic viewpoint. MRA should be employed for follow-up because of its applicability for outpatients, reasonable cost, and low risk.

DISADVANTAGES OF MRA

1) Poor spatial resolution

The spatial resolution of MRA is poor compared to other imaging methods, and subtle stenosis and irregularities of the walls may not be identified.

2) Walls cannot be visualized with routine MRA

Since MRA is a luminography, lumens are visualized, but walls are not. The addition of IVUS may be necessary to evaluate the vascular wall before intervention. The importance of imaging the wall in MR has been increasingly recognized, and plaque imaging has been attempted,⁵⁾ but no general plaque evaluation method has been established yet. Recently, for the coronary artery, evaluation of not only narrowing of the vascular lumen but also atheroma of the wall has been attempted to identify whether atheroma is likely to rupture. Although it is less necessary for the aorta compared to that for the coronary artery, cerebral infarction caused by rupture of atheroma of the aortic arch has been reported. Therefore, it is useful to know the severity of aortic atheroma before stenting. In the current situation, at least axial T1-weighted images (fat suppression imaging is desirable) should be additionally acquired (before and after contrast imaging), and black blood technique or diffusion-weighted images should also be acquired, if possible.

3) The presence or absence of wall calcification cannot be identified

CT may be employed for diagnosing aortic dissection, where deviated calcified intima or media may be a clue to its diagnosis, but it is less likely that information on calcification is essential for enhanced MRI.

4) Evaluation of the stent-placed region is impossible

When a metal stent is placed, local signals of the stent-contacted arterial wall are lost. The patency of the stented region can be evaluated only by assessing the upstream or downstream regions of the stent and based on collateral vessel formation.

5) Contraindications of MR

There are contraindications characteristic to MR, such as placement of a cardiac pacemaker or other metal devices.

6) Direct transition to intervention from imaging is impossible

At present, MR guided stenting and balloon angioplasty remain at an animal experimental level.

7) Caution is necessary for applications in renal failure patients

There is a risk of nephrogenic systemic fibrosis (NSF) in contrast-enhanced MRA, although it is small. In Japan, the incidence of NSF is one in 1000000 administration of gadolinium chelates, estimated from the consumption of gadolinium contrast media. Although single dose has routinely been used in many Japanese institutions, a double dose, triple dose or more contrast medium has been used mainly in Western countries for contrast enhanced MRA with gadolinium chelate, aiming at high-quality imaging with less artifacts.⁶⁾ Whole body MRA has also become applied with improvement of the performance of MR devices. However, enhancement cannot be maintained in the lower limbs by a single dose as larger field of view was required, for which a large volume, such as 40–60 mL, of contrast medium was administered in some cases in Western countries. The problem of NSF occurred in the midst of this trend and held off administration of high-dose gadolinium.

Since chelated gadolinium preparation is mostly non-nephrotoxic as long as it is intravenously administered, chelated gadolinium contrast media should be prioritized over iodinated contrast media for patients with a predisposition to renal dysfunction. Inversely, for patients who have completely lost renal function, examination using an iodine contrast medium should be prioritized, rather than gadolinium.

The incidence of NSF may be very low as long as administration at the normal dose (0.1 mmol/kg) is complied with.⁷⁾ The risk of NSF increases when eGFR is 30 mL/min/1.73 m² or lower.

MR IMAGER

Since the static magnetic field strength is proportional to the expected signal-to-noise ratio (SNR), high-field devices are desirable for MRA. It has been reported that the SNR of MRA images acquired using a 3-Tesla device, which has recently been introduced, is more favorable than that acquired using a 1.5-Tesla device. Since shorter repetition (TR) and echo (TE) times are desirable, a high-performance gradient system is desirable. When TR is short, longitudinal magnetizations of the background tissue are not given time for relaxation. Thus, the background signal is almost 0, increasing vascular contrast, and a short TE reduces the phase disruption of blood flow in voxels of acquired images and retains blood flow intensity.

To improve SNR, it is desirable to combine surface coils possessing independent receivers. The first purpose of this is to improve SNR, but it is also useful to increase temporal resolution by combining parallel imaging and reduce SAR at 3 Tesla, mainly by reducing RF power. Some recent models of MR acquisition systems are equipped with surface coils covering a long range in the cephalocaudal direction, in which coil attachment and detachment are not necessary even when images are acquired while sliding the table. Installed coils are sequentially activated from the upper toward the lower region with table movement. Combining multichannel surface coils with the recent high-speed acquisition technique, parallel imaging (such as SENSE and SMASH), the acquisition time can be shortened, or favorable spatial resolution can be obtained even if the acquisition time is the same.

As the latest technique, a system to reduce signal interference through several transmitting and receiving coils using RF with different wavelengths (parallel transmission) has been published.

ACQUISITION TECHNIQUE

MRA are roughly divided into 2 types: contrast and non-contrast MRA. Previous standards of non-contrast MRA included time-of-flight method and phase contrast method, however; investigations of the practical use of

non-contrast methods has recently been making progress, such as a method utilizing cardiac phase shifts of systolic and diastolic phases and a method utilizing spin labeling. Previously, providing reliable and stable vascular visualization by employing contrast-enhanced MRA was the main trend, and various modifications have been made, but physicians came to hesitate to apply contrast-enhanced MRA to patients who had lost renal function after the problem of NSF emerged. In this context, non-contrast MRA has recently been attracting attention.

Since arterial diseases are systemic diseases, it is desirable to include all arteries in the body including the aorta in the field of view.

1) Contrast-enhanced MRA (field of view and temporal resolution)

a) Table-moving MRA (also termed moving bed MRA, smart step MRA, or bolus chase MRA)

In this procedure, contrast-enhanced MRA of a large field of view can be acquired on a single injection of contrast medium while shifting the field of view from the abdominal through the pelvic, femoral, and calf regions. Bolus injection of contrast medium is necessary for imaging the abdominal region. When the intra-arterial contrast medium concentration reaches a specific level after this injection, contrast medium is then additionally administered at a dose to maintain the intra-arterial concentration level for subsequent imaging of the lower limbs. Infusion can be set at a low rate of 0.5–1.0 mL/s. It is possible to acquire an arteriogram of almost the whole body by connecting images of several regions, but this method is basically capable of acquiring MRA of only a single time phase. Thus, the patency of visualized arteries can be confirmed with this method, but non-visualized arteries is not necessarily proved occluded. Information concerning the flow direction is also impossible for this single-phase imaging.

b) Multiphase contrast MRA (repetitive acquisition of high-speed MRA in a specific region)

To acquire favorable images of contrast-enhanced MRA, it is necessary to maintain the intra-arterial contrast medium concentration above a certain level at least during low-frequency data filling in the k-space. When the acquisition time of a single phase was long, such as 20–30 seconds, the method to identify the contrast medium arrival time to the artery was important, but, with the improvement of MR devices and speed-up of

acquisition, time-resolved-MRA, in which 3-dimensional data collection is repeated and subtracted from those before contrast imaging, has become the main procedure, and the optimum contrast timing is no longer missed. Since temporal resolution is added to 3-dimensional imaging in this method, it is also termed 4D MRA or 3D MRDSA. For the pulse sequence, the sequence employed for contrast-enhanced MRA of the aorta is normally used. Field of view is shifted toward the caudal side after multiphase acquisition of the abdominal through pelvic region employing subtraction, and contrast medium is separately injected to visualize the lower limbs, the influence of the firstly injected contrast medium can be mostly eliminated. In multiphase contrast MRA, the optimum acquisition timing in the time-course intra-arterial contrast medium concentration is not missed, but a small matrix has to be inevitably set to increase temporal resolution, which may reduce spatial resolution due to trade-off. Attention should be paid to this when evaluating subtle collateral vessels and narrowed regions. This time-resolved method added temporal resolution to MRA and enabled identification of the blood flow direction, distinguishing true and pseudolumens of arterial dissection, from which arteries of organs branch, and the entry and re-entry positions and their patency. This is important information for surgical procedures and stenting. Procedures for closing the pseudolumen may not be applicable when a blood vessel of a vital organ, such as the renal artery, branches from a pseudolumen.

c) Contrast medium administration method

On contrast-enhanced MRA, higher contrast images can be acquired as the dose of contrast medium increases, if the cost or indications are not considered.⁸⁾ In Western countries, double-dose (0.2 mmol/kg) and triple-dose (0.3 mmol/kg) are adopted in many cases. Our facility performs multiphase imaging employing the 3D TRICKS method using contrast medium at 0.1 mmol/kg when only the lower limbs are imaged. When an extensive region is included, such as the abdominal through the pelvic region and lower limbs, gadolinium preparation is used at 0.15–0.2 mmol/kg up to a maximum volume of 20 mL in many cases. In the injection program employing the smartstep or moving table method, 0.1 mmol/kg of contrast medium is infused at 1 mL/s for the abdominal through pelvic region, followed by infusion of the remaining 0.05–0.1 mmol/kg of contrast medium at 0.5 mL/s for the lower limbs to maintain the intra-arterial concentration. However, only a single time phase can be imaged using

this smartstep or moving table method. When multiphase contrast MRA is applied in two regions: upper (pelvic-femoral region) and lower (femoral-calf region), bolus injection of 0.075–0.1 mmol/kg of contrast medium at 1 mL/s is applied to each region, and multiple phases are imaged.

The smartstep or moving table method is applied to determine the timing,⁹⁾ in which the contrast medium concentration upstream of the target artery is detected, and the MR device automatically starts the main scan when the intensity level within the aorta exceeds a specific point. In the fluoro-trigger method, high-temporal resolution prescan is repeated, the level in the target artery is visually observed in the image, and the main scan is started when an operator think the signal in the target vessel exceeded aspecific level. In the test-bolus method, prior to the examination, a small dose of contrast medium is firstly injected, the aortic signal level is observed, and the time required for reaching the maximum level is measured. This method adjusts the timing so that the main scan starts at the measured time after contrast medium administration. However, when temporal resolution is high, the above methods are unnecessary because MRA acquired at the optimum timing can be selected after imaging several phases.

2) Non-contrast MRA

Even though the cost and safety are considered, it is the best to visualize blood vessels without a contrast medium if possible, but the problems are reliability and stability. It is difficult to optimize many factors to achieve favorable visualization, and in some cases, non-contrast MRA has not been successful with several trials. As described above, the visualization capability of non-contrast time-of-flight MRA was insufficient in either 2D or 3D, but with the ECG-gated 3D half-Fourier fast-spin-echo method, visualization of the peripheral arteries has been accomplished by subtracting the dephasing from the rephasing image (by concomitantly using spoiler-pulse). In addition, arterial spin labeling utilizing inversion recovery pulse has been attempted with the use of balanced FFE, another acquisition method for MRA due to recent improvement of the gradient system performance.

Contrast-enhanced MRA is capable of selectively visualizing arteries by combining bolus intravenous injection of contrast medium to visualize early perfusion. To apply non-contrast MRA to the trunk and extremities, selective visualization of arteries and veins should



Fig. 2 Non-contrast MRA of the whole body (3D MIP projection). This angiogram is composed of several noncontrast MRA. Selective visualization of the arteries is well demonstrated without overlaps of veins.
MRA: magnetic resonance angiography;
MIP: maximum intensity projection

be accomplished with a principle different from that of contrast-enhanced MRA. Selecting and combining several non-contrast MRA methods in consideration of the magnetic field homogeneity, vascular distribution, and blood flow velocity enable vascular imaging of the whole body without a contrast medium (**Fig. 2**). There are diverse non-contrast MRA methods. Of these, several general methods involving 1.5T MRI of GE Healthcare (GEHC) and its application software are introduced below:

a) Flow preparation (flop prep) method

Arteries and veins are separated based on differences in the blood flow velocity and direction.¹⁰⁾ The maximum in-flow effect can be obtained by applying RF pulse at the time of the maximum arterial blood flow velocity, visualizing arterial blood with a high signal intensity. In contrast, venous blood with a slow flow velocity is excited to only a low level, resulting in a low signal intensity. Arteries and veins can be separated utilizing this difference in the signal intensity (**Fig. 3**). In clinical settings, firstly, the maximum flow velocity in the target blood vessel and the time required for reaching the maximum flow velocity after the R wave (delay time) are determined employing the phase contrast cine method (FAST card) (acquisition time: 15–20 seconds), followed by determining the optimum velocity encode (VENC). In the abdominal region, respiratory gating is also employed, and the acquisition time is about 2–4 minutes. This acquisition method is capable of vascular imaging over a broad range in a coronal section, and aneurysms, the abdominal aorta without dissection, and the common iliac, internal and external iliac, celiac, and renal arteries can be visualized (**Fig. 4**). When the blood flow is extremely slow in aortic aneurysm and dissection, and when different blood flow velocities exist at the same time, imaging employing the conventional flow prep method is difficult, and modified acquisition methods, such as addition and subtraction, are necessary to achieve a total view.^{11, 12)}

b) In-flow inversion recovery (IFIR) method

The name of this method was recently changed to the inherent enhancement inflow inversion recovery method (inherent inflow IR). This method utilizes the in-flow effect of blood (**Fig. 4**).^{13, 14)} The Time-slip method is well known as a preceding technique utilizing the same principle.¹⁵⁾ Inversion pulse is applied to a selective region including the target blood vessel to reduce the intensity of the background and non-imaged blood vessels. Selective imaging is possible by observing the in-flow effect of blood without inversion pulse in the target vessel. Devising setting of the inversion pulse in consideration of imaged vascular distribution, the blood flow velocity-independent selective imaging of arteries and veins is possible. However, the duration of an in-flow effect is limited. Imaging of a broad range is possible for blood vessels with a high flow velocity, but the range is narrowed when blood flow is slow because the distance reached per unit time is short. The distance reached by blood can be extended by setting a relatively long delay

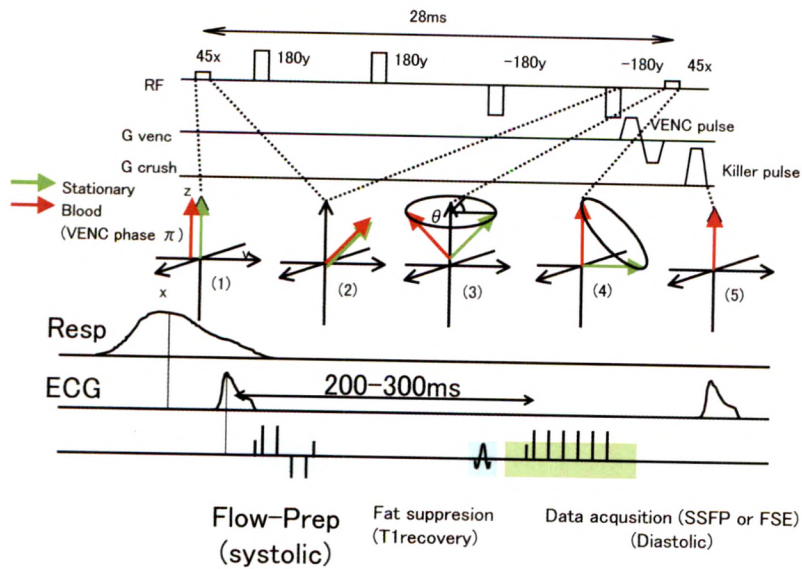


Fig. 3 Pulse sequence chart of Flow-prep MRA. Selective excitation of the arterial flowing blood can be performed with the use of velocity-encoding pulses.



Fig. 4 The flow-prep MRA technique demonstrates a wide range of the abdominal aorta and both renal arteries without overlap of the veins, especially around the periphery of the renal arteries in the case of the renal tumor (3D MIP reconstruction).

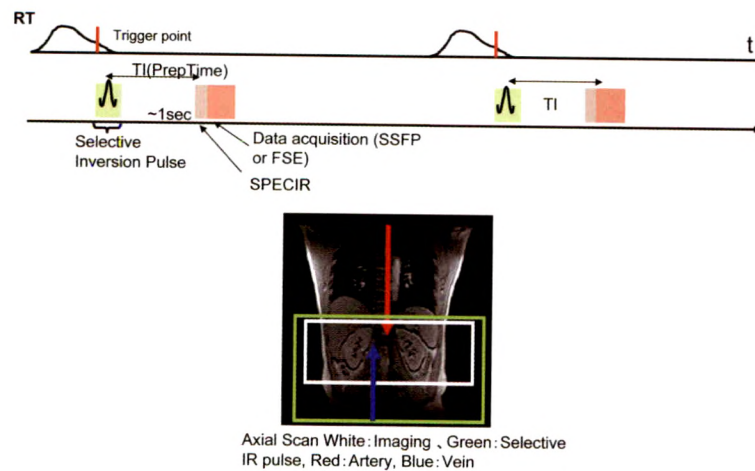


Fig. 5 Scheme of Enhance Inflow, IR: A selective IR pulse suppresses the signal of the vein and stationary tissue. Unsaturated fresh arterial blood can be visualized based on the inflow phenomenon, and selective visualization of the artery can be conducted. This scheme can be applied in any area in combination with SSFP or FSE.

time after inversion pulse application, but the contrast to blood vessels is reduced due to trade-off because the background intensity recovery increases in a time-dependent manner. This method is applicable for both Fast Imaging Employing Steady-State Acquisition (FIESA) and FSE of the SSFP system (**Fig. 5**), and differentially employed depending on the magnetic field homogeneity

and blood flow velocity.

c) Fresh blood imaging (FBI) method

This method utilizes differences in blood flow intensity between the systolic and diastolic phases. Only arteries are visualized by subtracting the systolic-phase venous image from the diastolic-phase arteriovenous image. This

is relatively common as a non-contrast MRA method.¹⁵⁾ When the blood flow velocity shows downstream of the stenosis region, blood vessels may not be accurately imaged. The absence of a need to be concerned with the adverse effects of contrast medium is an advantage of non-contrast MRA, as described above. In contrast-enhanced dynamic MRA, images can be acquired only at a single timing per test, and when the timing is missed, imaging fails and reading and diagnosing may be difficult. In contrast, in non-contrast MRA, acquisition can be repeated while changing the optimum condition during a single test, resulting in reducing non-assessable cases. It has also been reported that the separation of arteries and veins and background inhibition independent from the timing of contrast medium circulation achieved favorable imaging of the renal artery compared to contrast-enhanced MRA.^{11, 13)} Furthermore, the acquisition methods of non-contrast MRA realize the visualization of flow, which may image not only blood vessels but also flowing fluids. The proposition of the development of non-contrast MRA in the future is shortening of the acquisition time while imaging blood vessels in a broad range, for which the development and devising of acquisition methods and operation are expected.

RECONSTRUCTION

Generally, acquired images of contrast-enhanced MRA are reconstructed after subtracting the mask images (original images before enhancement) from the enhanced images. The images after subtraction are reconstructed employing the maximum intensity projection (MIP) or sliding MIP (multiplanar volume reconstruction (MPVR)) methods. Separately, it is necessary to observe the original images before and after enhancement and specific serial cross-sections employing multi planar reformat (MPR).

RENAL DYSFUNCTION AND INDICATIONS OF CONTRAST-ENHANCED AND NON-CONTRAST MRA

When an arterial or venous disease is suspected but physicians hesitate to use iodinated contrast media because of allergy, or when the Seldinger technique of the catheter approach is not applicable, these cases are appropriate indications of MRA. Indicated diseases include almost all diseases accompanied by vascular lesions, such as arteriosclerosis obliterans (ASO), Buerger disease (thromboangiitis), aneurysm (true and false), arteriovenous fistula, arterial dissection,, for which the usefulness

of contrast-enhanced MRA and favorable outcomes have been reported by many researchers.¹⁶⁻²²⁾ When renal function is lost, contrast-enhanced imaging using an iodinated contrast medium or non-contrast MRA should be selected on the condition of dialysis, but when renal dysfunction is moderate or milder, for the remaining renal function to be conserved; contrast-enhanced MRA should be selected. When aortitis or inflammatory aneurysm is suspected, contrast enhancement is obviously essential.

VASCULAR WALL IMAGING

The techniques discussed above are luminographic techniques, regardless of contrast-enhanced or non-contrast MRA. Studies on responsible arteries for myocardial and cerebral infarctions have clarified that there are stenoses with favorable and poor prognoses (stable and unstable plaques, respectively) in arteriosclerotic stenosis, and differentiation of the plaque type in the vascular wall is necessary to differentiate these. The vascular wall cannot be observed employing luminography, and the black-blood method is basically used for this evaluation. For vascular wall imaging, the method in which data collection is started from the null-point of blood employing the non-selective IR preparation pulse is widely employed.²³⁾ USPIO accumulated by macrophages and other tissue-specific contrast media are also utilized in laboratory experiments.

RELATIONSHIP BETWEEN BLOOD FLOW AND THE VASCULAR WALL (IMPORTANCE OF FLOW ANALYSIS)

As a characteristic of MRI, the flow velocity can be quantitatively evaluated, in which the magnetic field gradient is spatially loaded, and flow-induced phase shifts of spin are measured as changes in signal intensity. Data were previously collected only in the 2-dimensional cross-sections, but, employing 3-dimensional data collection and ECG gating for all phases of the cardiac cycle, the flow velocity can be measured in all phases in all intravascular regions within the region of interest in-vivo by collecting data in all phases. Time-resolved 3-dimensional phase-contrast MRI (4D Flow) capable of collecting blood flow data in 3-dimensional space and time, 4 dimensions in total, has been developed and facilitated the application of blood flow analysis in various blood vessels.^{24, 25)} By analyzing data of 4D Flow using flow analysis software, flow visualization and analysis (Flava), for example, blood flow measurement in vital

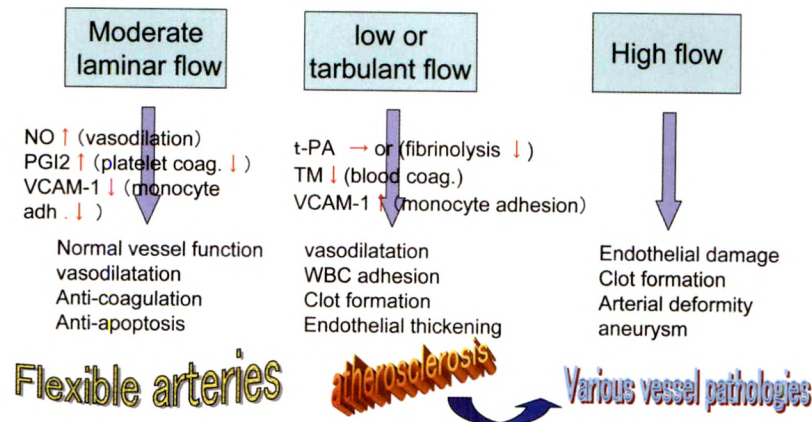


Fig. 6 The effect of shear stress on the vessels.

There are several hypotheses concerning the effect of physical stimuli like shear stress on the vessels.

The diagram shows one of the recent and widely accepted hypotheses.

Moderate and appropriate shear stress detected by the endothelium increases NO in the vessel wall and, thereby, dilates vessels and, at the same time, increases PGI2, which inhibits platelet coagulation, and decreases VCAM-1, which inhibits monocyte adhesion. These are anti-arteriosclerosis factors. For the integrity of the vessel wall, wall shear stress should be maintained at an appropriate level of not less than 1.5 Pa. A low shear stress below 0.4 Pa promotes atherosclerosis and the apoptosis of smooth muscle in the vessel wall.

organs and analysis of the blood flow direction and blood flow measurement in grafts can be performed.

The presence of flow velocity data in time and space indicates that endothelial shear stress can be measured in the vascular wall. Various factors are related to the development and progression of vascular lesions. In addition to vascular wall vulnerability associated with hyperlipidemia, diabetes, cigarette smoking, and Marfan syndrome, hemodynamic factors are also present. On the other hand, there are regions likely to develop vascular lesions. Arteriosclerotic changes frequently occur in the coronary artery, bifurcations of the carotid artery and abdominal aorta at peripheral sides from the renal arteries. Cerebral aneurysms also have predilection sites. These facts suggest the importance of hemodynamic factors. Of hemodynamic factors, the association between vascular wall shear stress and vascular lesions has been widely studied. In the velocity distribution of intravascular blood flow, the speed is high in the central region, but slow near the vascular wall, forming a velocity gradient (shear rate). The friction force that the vascular wall receives from blood is called shear stress, presented with the following equation:

$$\tau = \mu (dv/dx)$$

τ : Shear stress, μ : viscosity (about 3.9×10^{-3} Pa·sec in

human blood), dv/dx : shear rate

Vascular endothelium reacts with the vascular wall shear stress in various ways. Morphologically, loading an about 1.5-Pa shear stress on the vascular epithelium causes a spindle-pattern arrangement in parallel to the flow direction. Functionally, a physiological shear stress greater than 1.5 Pa acts against arteriosclerosis through reducing vasoconstrictor production, increasing vasodilator and antioxidative enzyme production, reducing growth factor expression, increasing growth inhibitor expression, and reducing inflammatory mediator and adhesion molecule expression, thrombus formation, and epithelial growth ability. In contrast, a low shear stress below 0.4 Pa and varying shear stress direction with time due to turbulence are known to act on vascular epithelium leading to arteriosclerosis.^{26, 27)}

Involvement of shear stress of the vascular wall in aneurysm occurrence is also suspected. An aneurysm is likely to develop at the proximal vascular bifurcation in patients following ligation of the unilateral carotid artery,²⁸⁾ suggesting that an increase in vascular wall shear stress with increases in the blood flow and velocity is related to aneurysm occurrence. It has recently been considered that vascular wall shear stress is closely related to vascular degeneration through iNOS and NO. The association of vascular wall degeneration and apoptosis

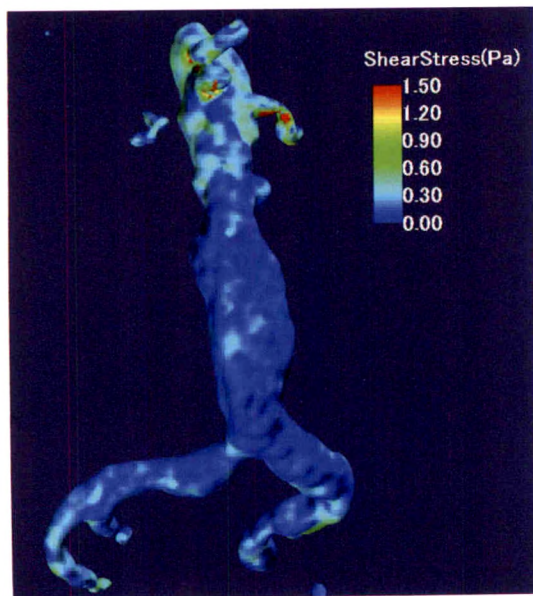


Fig. 7 Color coded display of a shear stress map generated in an elderly patient with an infra-renal abdominal aortic aneurysm. Note the significantly lower shear stress below 0.3 Pa in the diffusely dilated segments around the bifurcation of the aorta. This aneurysm developed as a result of the hemodynamic mechanism explained in Fig. 6.

induced by low vascular wall shear stress with aneurysm rupture is also discussed. For long-term prospects, the investigation of arterial wall health by analyzing shear stress and prediction of the long-term progression of arterial lesions are considered (Figs. 6 and 7).

If hemodynamic analysis can be applied to predict sites at which arteriosclerosis occurs in the future, it is possible to predict vascular lesions beforehand. The previous paradigm was the discovery and removal of already formed vascular lesions and its follow-up, but if the association between the shear stress and development of vascular lesions can be sufficiently elucidated in vivo, the prediction and prevention of arterial lesions may become the future trend.

READING AND INTERPRETATION OF MRA

Firstly, images reconstructed employing MIP are observed in many directions to outline blood vessels. Dilated and narrowed segments are then evaluated in detail employing MPR and MPVR to confirm the presence or absence of collateral blood vessels, which may facilitate the accurate evaluation of collateral blood vessels and narrowed regions undetectable by employing MIP alone.

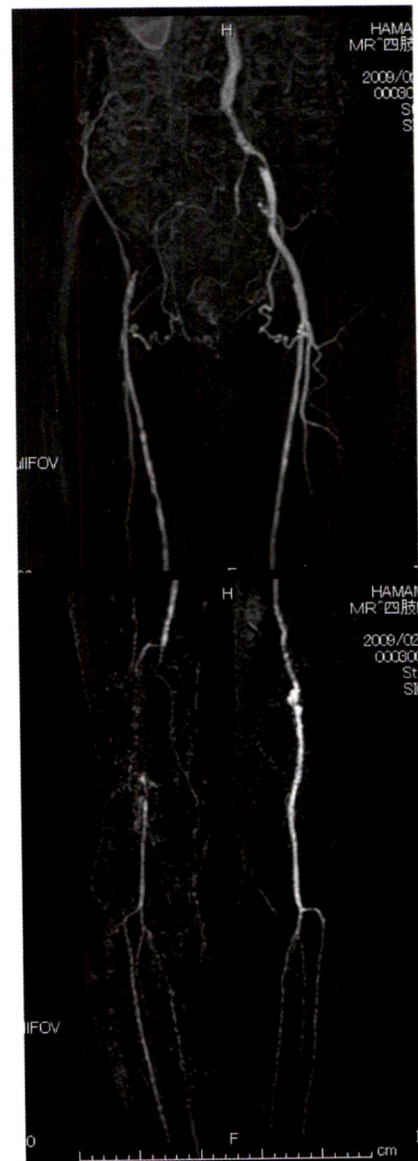


Fig. 8 Three-dimensional MIP projection image of contrast-enhanced MRA of an elderly male patient with arteriosclerosis obliterans, showing total occlusion of the right common iliac artery and right external iliac artery. The right lower limb is dependent on cross circulation through the left internal iliac artery. The popliteal artery is also near-occluded on the right side. Bypass surgery is not indicated for patients with a similar condition. Alternative therapy such as pharmacological intervention is chosen. MIP: maximum intensity projection; MRA: magnetic resonance angiography

For bypass surgery, PTA, and stenting, confirmation of the presence or absence of run-off is necessary (Figs. 8 and 9). Multiphase MRA is acquired in as many phases as possible to avoid overlooking findings. It is also necessary to observe the upstream aorta. The original



Fig. 9 Three-dimensional MIP projection image of contrast-enhanced MRA of an ASO patient showing occlusion of the left common iliac artery, left superficial femoral artery, and severe stenosis of the right external iliac artery. If the “run-off” of popliteal arteries and trifurcations as well as further peripheral arteries are maintained, bypass surgery is indicated, as in this patient.
MIP: maximum intensity projection;
MRA: magnetic resonance angiography;
ASO: arteriosclerosis obliterans

images are also confirmed. When an aneurysm is present, mural thrombus is investigated, and the stent position is confirmed based on the presence of metal artifacts. It is needless to say that reviewing CT and surgical records is also necessary.

Furthermore, inflammatory aneurysm (**Fig. 10**), aortitis

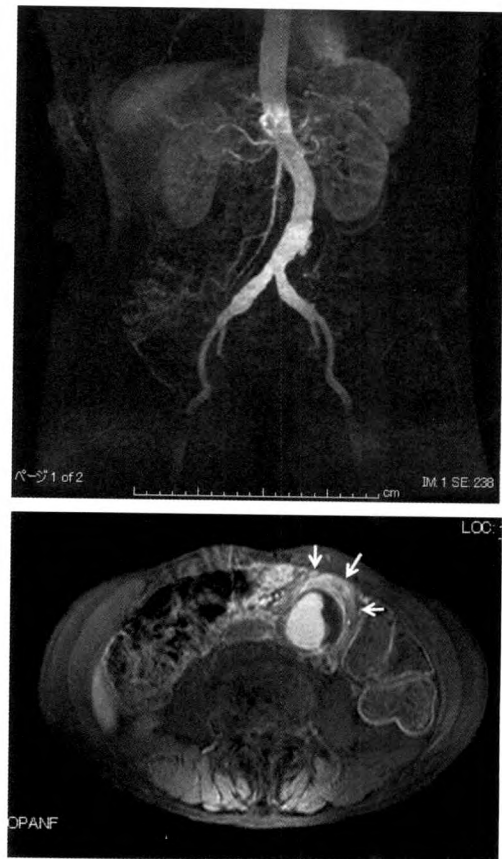


Fig. 10

a: Elderly male patient with an infected aneurysm in the abdominal aorta (3D MIP projection MRA using contrast-enhanced MRA).

There is an ulcer on the left side of the aorta just above the bifurcation.

b: Axial fat-saturated T1-weighted image with gadolinium enhancement. There is a strong enhancement in the soft tissue layer surrounding the abdominal aorta (→).

MIP: maximum intensity projection;

MRA: magnetic resonance angiography;

(**Fig. 11**), and Behcet’s disease, IgG 4-related diseases, and wall inflammation can be detected as enhancement by contrast medium by adding fat-suppressed T1-weighted cross-sectional imaging subsequently to contrast-enhanced MRA.

MRA displays its power in postoperative follow-up, such as tracing the presence, enlargement, and shrinkage of ULP (**Fig. 12**) and PAU (**Fig. 13**).

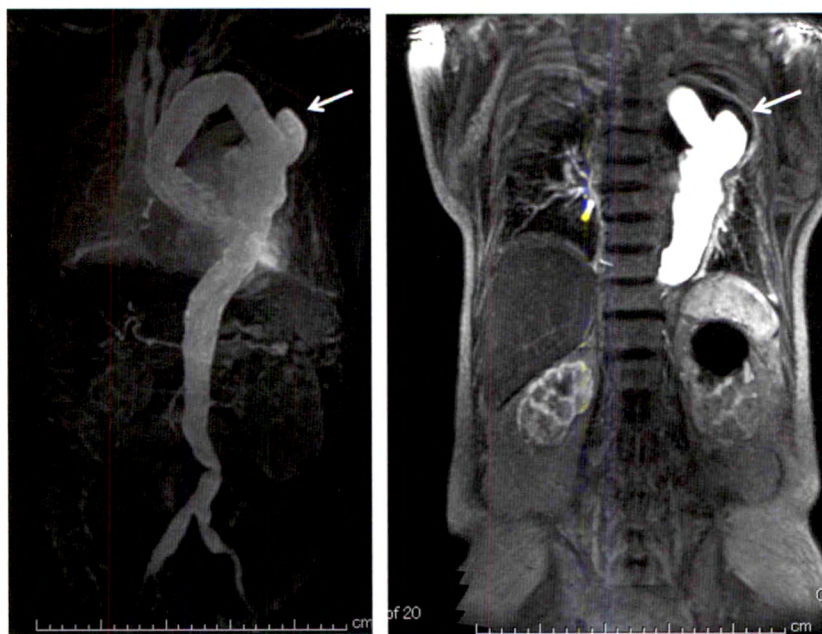
For aortic dissection, true and pseudolumens and the blood flow condition of the branching arteries can be investigated by high-temporal resolution imaging (**Figs. 14 and 15**).



Fig. 11 Middle aged female patient with aortitis syndrome (3D MIP projection image using contrast-enhanced MRA). There is a short segment of stenosis at the infrarenal segment of the abdominal aorta (→) followed by distal post-stenotic dilatation.
MIP: maximum intensity projection;
MRA: magnetic resonance angiography



Fig. 12 Contrast-enhanced MRA (left anterior oblique view; 3D MIP projection) of a patient with thrombosed-type Stanford B aortic dissection. There are several ULP at the distal portion of the aortic arch (→).
MIP: maximum intensity projection;
MRA: magnetic resonance angiography;
ULP: ulcer-like projections



a | b

Fig. 13
a: Growing PAU (→) seen in the thoracic aorta of an elderly male patient (left anterior oblique view; 3D MIP projection) Contrast-enhanced MRA. Risk of rupture increased in this case.
b: Coronal source image shows a huge ulcer created due to atherosclerosis in the thoracic descending aorta.
PAU: penetrating atherosclerotic ulcer;
MIP: maximum intensity projection;
MRA: magnetic resonance angiography



a | b

Fig. 14

a: Enhanced MRA showing dissection in the thoraco-abdominal aorta (3D MIP projection).

Three main visceral arteries (→) (the celiac axis, superior mesenteric artery, and left renal artery) stem from the true lumen. Right renal artery branches from the pseudolumen (*) remain unoccluded.

b: Precontrast fat-saturated coronal T1-weighted image. Dissected pseudolumen in the thoracic aorta almost occluded with thrombosis. MIP: maximum intensity projection; MRA: magnetic resonance angiography



a | b

Fig. 15

a: Pseudoaneurysm (contrast leakage into the pseudolumen) seen in the elderly male patient, which was created at the orifice of the celiac axis after graft replacement (left anterior oblique MIP projection of the contrast-enhanced MRA).

b: Oblique coronal reconstruction of the source image shows the pseudoaneurysm outpouching from the celiac axis.

MIP: maximum intensity projection;

MRA: magnetic resonance angiography;

Dissemination of dissection to branching arteries and multiple aneurysm development with aortic lesions have recently been frequently encountered. MRA also plays an important role in planning interventions for these lesions and later evaluation.

PITFALL IN OBSERVATION OF MRA

When a metal stent is placed in a blood vessel, signals in the stented region are lost and may be perceived as a pseudostenosis. Moreover, MRA normally visualizes only lumens because of subtraction. A mural thrombus may be overlooked when only MRA following MIP reconstruction is observed. Observation of multiple cross-sections of the original images before subtraction should be routinely performed. It is also necessary to confirm the procedure applied before MRA in patients after bypass surgery, otherwise bypass graft near the body surface may be excluded from the field of view. Furthermore, as described above, when the optimum acquisition timing is missed, non-visualized blood vessels may be misidentified as obstruction. This can be avoided by multiphase acquisition.

There are reasons why noninvasiveness is desirable for the imaging of vascular lesions. Firstly, repeated examination is necessary for patients with vascular lesions. Arterial lesions are exposed to blood flow stress daily and go through dynamic morphological changes. When a vascular lesion is already present, it is necessary to not only pay attention to its progression, but also follow the course after surgical treatment by imaging because such changes progress, for which invasiveness and the nephrotoxicity of contrast medium are not desirable. For example, when an arterial lesion is surgically repaired, reportedly, an aneurysm is formed at a site distant from the surgically repaired site within 18–24 months in 17%–25% of cases. It has also been pointed out that an ulcer-like projection may cause recurrence of dissection and aneurysm formation, and become a starting point of rupture. It is also known that the enlargement of an abdominal aortic aneurysm is accelerated when the diameter exceeds a certain size (0.6 cm or greater enlargement after the diameter exceeds 6 cm).²⁹⁾

CONCLUSION

Contrast-enhanced MRA has been refined with the advancement in MR technology, and images with high temporal as well as spatial resolutions have been acquired.

Cases in which X-ray angiography is non-applicable, high-risk cases, and cases requiring frequent follow-ups are appropriate indications of MRA. Non-contrast MRA techniques have also recently advanced, for which safe MRA for patients with renal failure can be expected. Development of the 3D cine PC method facilitated application of hemorheological analysis for the evaluation of shear stress of the wall. The prediction and prevention of arteriosclerotic lesions as vascular wall lesions may become possible in the future.

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REFERENCES

- 1) Nash K, Hafeez A, Hou S. Hospital-acquired renal insufficiency. *Am J Kidney Dis* 2002; **39**: 930-6.
- 2) Prince MR, Arnoldus C, Frisoli JK. Nephrotoxicity of high-dose gadolinium compared with iodinated contrast. *J Magn Reson Imaging* 1996; **6**: 162-6.
- 3) Nyman U, Elmstahl B, Leander P, et al. Are gadolinium-based contrast media really safer than iodinated media for digital subtraction angiography in patients with azotemia? *Radiology* 2002; **223**: 311-8, discussion 328-9.
- 4) Bridges MD, St Amant BS, McNeil RB, et al. High-dose gadodiamide for catheter angiography and CT in patients with varying degrees of renal insufficiency: Prevalence of subsequent nephrogenic systemic fibrosis and decline in renal function. *AJR Am J Roentgenol* 2009; **192**: 1538-43.
- 5) Fayad ZA, Fuster V. Clinical imaging of the high-risk or vulnerable atherosclerotic plaque. *Circ Res* 2001; **89**: 305-16.
- 6) Maki JH, Wilson GJ, Eubank WB, et al. Utilizing SENSE to achieve lower station sub-millimeter isotropic resolution and minimal venous enhancement in peripheral MR angiography. *J Magn Reson Imaging* 2002; **15**: 484-91.
- 7) Prince MR, Zhang H, Morris M, et al. Incidence of nephrogenic systemic fibrosis at two large medical centers. *Radiology* 2008; **248**: 807-16.
- 8) Mitsuzaki K, Yamashita Y, Ogata I, et al. Optimal protocol for injection of contrast material at MR angiography: study of healthy volunteers. *Radiology* 1999; **213**: 913-8.
- 9) Foo TK, Saranathan M, Prince MR, et al. Automated detection of bolus arrival and initiation of data acquisition in fast, three-dimensional, gadolinium-enhanced

- MR angiography. *Radiology* 1997; **203**: 275-80.
- 10) Miyoshi M, Tsukamoto T. Flow preparation pulse for abdominal non-contrast-enhanced MR angiography. 2006 ISMRM.
 - 11) Masui T, Katayama M, Sato K, et al. Non Contrast MRA of renal artery using Flow-prep FIESTA for evaluation of patients with suspected renal tumor: Comparison of Dynamic contrast MRA, 2008 ISMRM.
 - 12) Masui KM, Miyoshi M, et al. Evaluation of the femoral arteries; before and after tumor treatments using non-contrast MRA using subtraction method based on velocity encoding Technique. 2009 ISMRM.
 - 13) Masui T, Katayama M, Sato K, et al. Evaluation of the renal arteries: comparison of two types of Non-contrast MRA and Dynamic contrast MRA, 2009 ISMRM.
 - 14) Sato K, Masui T, Katayama M, et al. Non-contrast-enhanced MR angiography of the carotid arteries and aortic arch using Inherent Enhancement (Inhance) Inflow IR, adopting peripheral-gated partial-Fourier fast spin echo (FSE) or steady-state Free Precession (FIESTA): A comparison with contrast MRA, 2009 ISMRM15).
 - 15) Miyazaki M, Sugiura S, Tateishi F, et al. Non-contrast-enhanced MR angiography using 3D ECG-synchronized half-Fourier fast spin echo. *J Magn Reson Imaging* 2000; **12**: 776-83.
 - 16) Yucel EK, Kaufman JA, Geller SC, et al. Atherosclerotic occlusive disease of the lower extremity: prospective evaluation with two-dimensional time-of-flight MR angiography. *Radiology* 1993; **187**: 637-41.
 - 17) Ralston MD, Dykes TA, Applebaum BI. Verification of lumbar vertebral bodies. *Radiology* 1992; **185**: 615-6.
 - 18) Kim D, Edelman RR, Kent KC, et al. Abdominal aorta and renal artery stenosis: evaluation with MR angiography. *Radiology* 1990; **174**(3 Pt 1): 727-31.
 - 19) Bland PH, DiPietro MA, Chenevert TL, et al. Tissue characterization of the testes using ultrasonic CT. Work in progress. *Radiology* 1986; **159**: 101-5.
 - 20) Glazer HS, Lee JK, Levitt RG, et al. Radiation fibrosis: differentiation from recurrent tumor by MR imaging. *Radiology* 1985; **156**: 721-6.
 - 21) Johnson DW, Voorhees RL, Lufkin RB, et al. Cholesteatomas of the temporal bone: role of computed tomography. *Radiology* 1983; **148**: 733-7.
 - 22) Herfkens RJ, Higgins CB, Hricak H, et al. Nuclear magnetic resonance imaging of atherosclerotic disease. *Radiology* 1983; **148**: 161-6.
 - 23) Song HK, Wright AC, Wolf RL, et al. Multislice double inversion pulse sequence for efficient black-blood MRI. *Magn Reson Med* 2002; **47**: 616-20.
 - 24) Yamashita S, Isoda H, Hirano M, et al. Visualization of hemodynamics in intracranial arteries using time-resolved three-dimensional phase-contrast MRI. *J Magn Reson Imaging* 2007; **25**: 473-8.
 - 25) Markl M, Chan FP, Alley MT, et al. Time-resolved three-dimensional phase-contrast MRI. *J Magn Reson Imaging* 2003; **17**: 499-506.
 - 26) Malek AM, Alper SL, Izumo S. Hemodynamic shear stress and its role in atherosclerosis. *JAMA* 1999; **282**: 2035-42.
 - 27) Ando J, Yamamoto K. Vascular mechanobiology: endothelial cell responses to fluid shear stress. *Circ J* 2009; **73**: 1983-92 Epub 2009 Oct 5.
 - 28) Dyste GN, Beck DW. De novo aneurysm formation following carotid ligation: case report and review of the literature. *Neurosurgery* 1989; **24**: 88-92.
 - 29) Brewster DC, Cronenwett JL, Hallett JW Jr, et al. Guidelines for the treatment of abdominal aortic aneurysms. Report of a subcommittee of the Joint Council of the American Association for Vascular Surgery and Society for Vascular Surgery. *J Vasc Surg* 2003; **37**: 1106-17.

Simultaneous Evaluation of the Whole Aorta and Artery of Adamkiewicz by MDCT

Kei Takase

Recent technical advancement has allowed simultaneous visualization of the artery of Adamkiewicz and whole aorta by multidetector-row-CT (MDCT). Although we could visualize the artery of Adamkiewicz in a high percentage of patients with thoracoabdominal aortic diseases, CT scanning with an adequate protocol and careful post-processing are necessary for accurate evaluation. Noninvasive evaluation of the artery of Adamkiewicz is useful in planning surgery. Preoperative evaluation of the intercostal arterial level from which the artery of Adamkiewicz originates is reportedly important for preventing postoperative spinal cord ischemia. Although, the usefulness of preoperative information on the artery of Adamkiewicz is still controversial, preoperative identification of the artery of Adamkiewicz by imaging has gradually spread since our first report, and has been included in preoperative evaluation items at many institutions, revealing its contribution to improvement in surgical results. (*English Translation of J Jpn Coll Angiol, 2004, 44: 693-699.)

Keywords: Adamkiewicz, aorta, MDCT, spine, aneurysm

INTRODUCTION

Multidetector-row-CT (MDCT) has spread to many institutions during the 13 year period since its appearance. MDCT is particularly useful for imaging the vascular system, enabling both vascular visualization over a wide range and detailed branching diagnosis, both of which were impossible using single slice helical CT. CT was conventionally used as a method complementary to angiography, but has replaced angiography. MDCT not only replaces angiography but also provides intuitive morphological information on 3-dimensional reconstruction images. In addition, this technique has enabled the

visualization of blood vessels in detailed areas such as the artery of Adamkiewicz, which is often difficult to evaluate even using angiography.¹⁻³⁾

Various factors are considered to be involved in the development of spinal ischemia after surgery of the thoracic or thoracoabdominal aorta. To prevent postoperative paraplegia, shortening of the spinal cord blood flow interruption time, combined use of assisted circulation (peripheral aortic perfusion, selective intercostal artery perfusion), intercostal artery reconstruction, cerebrospinal fluid drainage, and hypothermia are used. Basically, the prevention of postoperative spinal ischemia consists of the maintenance of spinal cord circulation and spinal protection. For the former, the preoperative identification of the artery of Adamkiewicz, which most markedly contributes to spinal cord blood supply in the thoracolumbar region, is useful.⁴⁻¹⁷⁾ Identification of the level of the intercostal or lumbar artery supplying the artery of Adamkiewicz enables the formulation of a surgical plan including the intercostal artery reconstruction level, reducing the operation time, and the preservation of the artery giving rise to the artery of Adamkiewicz or its surrounding arteries. In this study, concerning the preoperative identification of the artery of

Department of Diagnostic Radiology, Tohoku University School of Medicine, Sendai, Miyagi, Japan

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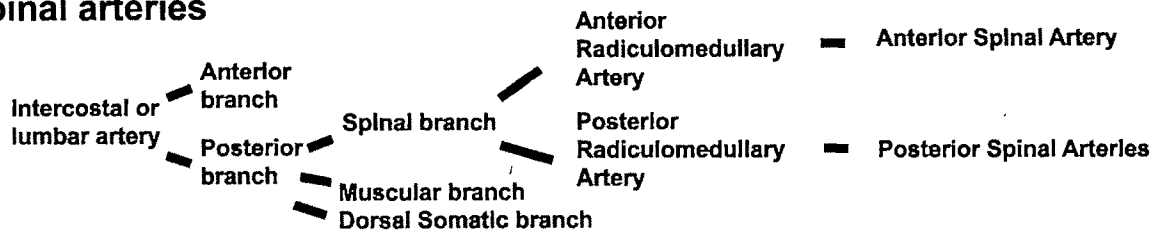
Corresponding author: Kei Takase. Department of Diagnostic Radiology, Tohoku University School of Medicine, 1-1 Seiryō, Aoba-ku, Sendai, Miyagi 980-0872, Japan

Tel: +81-022-717-7312, Fax: +81-022-717-7316

E-mail: ktakase@rad.med.tohoku.ac.jp

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Spinal arteries



Spinal veins

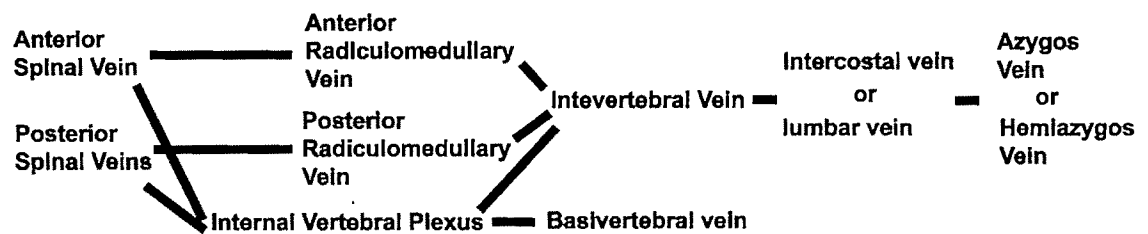


Fig. 1 Vascular anatomy of the spine.

Adamkiewicz using MDCT, the anatomy of the spinal cord arteries, and examination, image processing, and evaluation methods were described, and the clinical usefulness of visualization of the artery of Adamkiewicz was discussed.

ANATOMY

The branching patterns of the spinal arteries and veins are shown in Fig. 1.

The anterior spinal artery running longitudinally along the anterior median fissure of the spinal cord supplies the anterior 2/3 portion of the spinal cord, and the 2 posterior spinal arteries (one located on each side of the spinal cord posteriorly) supply the posterior funiculus. The anterior spinal artery is supplied by the anterior radiculomedullary arteries branching from the intercostal and lumbar arteries. Among the radiculomedullary arteries, the artery of Adamkiewicz is the largest. An autopsy study by Koshino et al. showed that this artery was located on the left side in 72% and between Th8 and L1 in 91%.¹⁸⁾ Since the anterior spinal artery is frequently thin cranial to the entry site of the artery of Adamkiewicz and thick caudal to this site,¹⁹⁾ CT often allows the visualization of only its caudal portion.

IMAGING METHODS

We devised a protocol for the simultaneous acquisition of information on the whole aorta and iliac artery and that

on the artery of Adamkiewicz, and used this protocol in patients with thoracoabdominal aortic diseases for which surgery is indicated. Adequate information on major blood vessels can be obtained only by CT performed once (so-called one-stop-shop examination). Our protocol and points in the examination are introduced below. Although there are various cautionary items due to the visualization of fine structures, the procedure can be reproduced if there is a 16-(or more) detector row MDCT scanner. With an increase in the number of detector rows of MDCT, the breath-holding time decreased while scan timing became more important.

The general examination procedure is as follows:

1. Preparation before scanning

Insertion of a 20G indwelling needle into the right basilic vein showing a favorable condition, or into the right external jugular vein when insertion into the basilic vein is impossible

Positioning to bring the vertebral body to the isocenter

2. Non-enhanced CT scanning of major blood vessels

3. Setting of the scan initiation timing

Since most models have a function to initiate scanning after sensing contrast agent arrival at the aorta, be sure to use this function.

First, the site of the monitoring scan for contrast agent arrival at the aorta is determined.

Next, the region of interest (ROI) is established in the superior portion of the descending aorta, and the scan initiation timing is set so that scanning can be initiated

at an intravascular CT value of about 150 HU.

4. Imaging in the early phase of contrast enhancement

According to body weight, about 100–120 mL of a contrast agent at a high concentration (350–370 mgI/mL) is used. The injection rate is set at 3.5–4.5 mL/sec. A blood vessel allowing bolus injection of the contrast agent is necessary, and contrast enhancement through the right external jugular vein is often performed. For the accurate visualization of the artery of Adamkiewicz in patients with major vessel disease, a rather high dose of the contrast agent is required, but slight adjustments are made according to the body weight, renal function, and aneurysm size. It is desirable to flush with saline injection following contrast agent injection using a dual injector.

The scan range is from the lung apex to the ischial tuberosity. The scan continuation time is set at about 20 seconds. Using the finest collimation (≤ 1 mm) of the scanner, the electric current is set high (about 350 mA).

Before the initiation of contrast enhancement, it is confirmed again using physiological saline that the contrast enhancement line allows injection without resistance or pain even at the planned injection rate, and it is explained again that patients become warm after contrast agent injection.

In some patients with aortic dissection, the artery of Adamkiewicz arises from a false lumen, or a slightly slow scan timing is appropriate. Therefore, re-scanning is performed after a breath-hold following scanning in the early phase of contrast enhancement. Although the high electric current and two scans increase the X-ray exposure dose, we permit this since the benefit of reducing the surgical risk due to the visualization of the artery of Adamkiewicz outweighs this drawback.

5. Imaging in the delayed phase

Imaging is performed to evaluate slow blood flow in the false lumen in patients with aortic dissection, the state of the walls of inflammatory aneurysms, and venous anatomy (such as the retroaortic renal vein).

6. Image reconstruction and processing

Image reconstruction using two types of field of view (FOV)

The following two types of image are produced. Short-axis images are produced for the whole aorta without narrowing the FOV. For the straightforward identification of the artery of Adamkiewicz, the FOV is narrowed to the aorta and perispinal area, increasing spatial resolution.

IMAGE PROCESSING ON THE WORKSTATION

We generally use the Aquarius net viewer (TeraRecon, Foster City, USA) for image interpretation, and the Ziostation (Amin, Tokyo, Japan) for detailed image processing. To readily identify the artery of Adamkiewicz on images, curved planar reformation (CPR) images from the aorta to the area along the intercostal artery, the artery of Adamkiewicz, and anterior spinal artery, is the most useful. As the previous stage of the production of this image, the artery of Adamkiewicz should be identified by detailed observation of the original animated short-axial image.³⁾ At the time of surgery, it is necessary to show the origin of the segmental artery (giving rise to the artery of Adamkiewicz) in the aorta using 3-dimensional images that can be straightforwardly understood by surgeons.

IDENTIFICATION OF THE ARTERY OF ADAMKIEWICZ AND ITS VISUALIZATION CAPACITY

When reconstruction is performed at 0.5-mm intervals, more than 1000 short-axis images are obtained. Therefore, at present, observation is performed using the paging method on the Workstation. On short-axis images, the anterior spinal artery is present on the ventral midline. The artery of Adamkiewicz enters this artery, and passes through the intervertebral foramen, running to the ventral side of the spinal cord (**Fig. 2E–2H**). On coronal images on cine-mode displays, since the artery of Adamkiewicz is continuous with the anterior spinal artery, forming a hair-pin curve, this structure is identified for the identification of the artery of Adamkiewicz. The level of the intervertebral foramen, through which the intercostal artery is continuous with this hair-pin curve structure, is counted from the sacral bone and regarded as the level of the artery of Adamkiewicz (**Fig. 2I–2J**). The most difficult problem for its identification is differentiation from the anterior radiculomedullary vein. The anterior spinal vein also shows morphology similar to that of the anterior radiculomedullary vein. Therefore, differentiation between the artery and vein is inaccurate based on morphological findings alone. The most accurate differentiation method is to visualize the continuity between the intervertebral/lumbar artery and artery of Adamkiewicz (**Figs. 2I–2J**). In our previous report, using 4-detector row MDCT with 2-mm collimation, we could identify the artery of Adamkiewicz in the spinal canal in 90% but could visualize the continuity between the intervertebral/lumbar artery and the artery

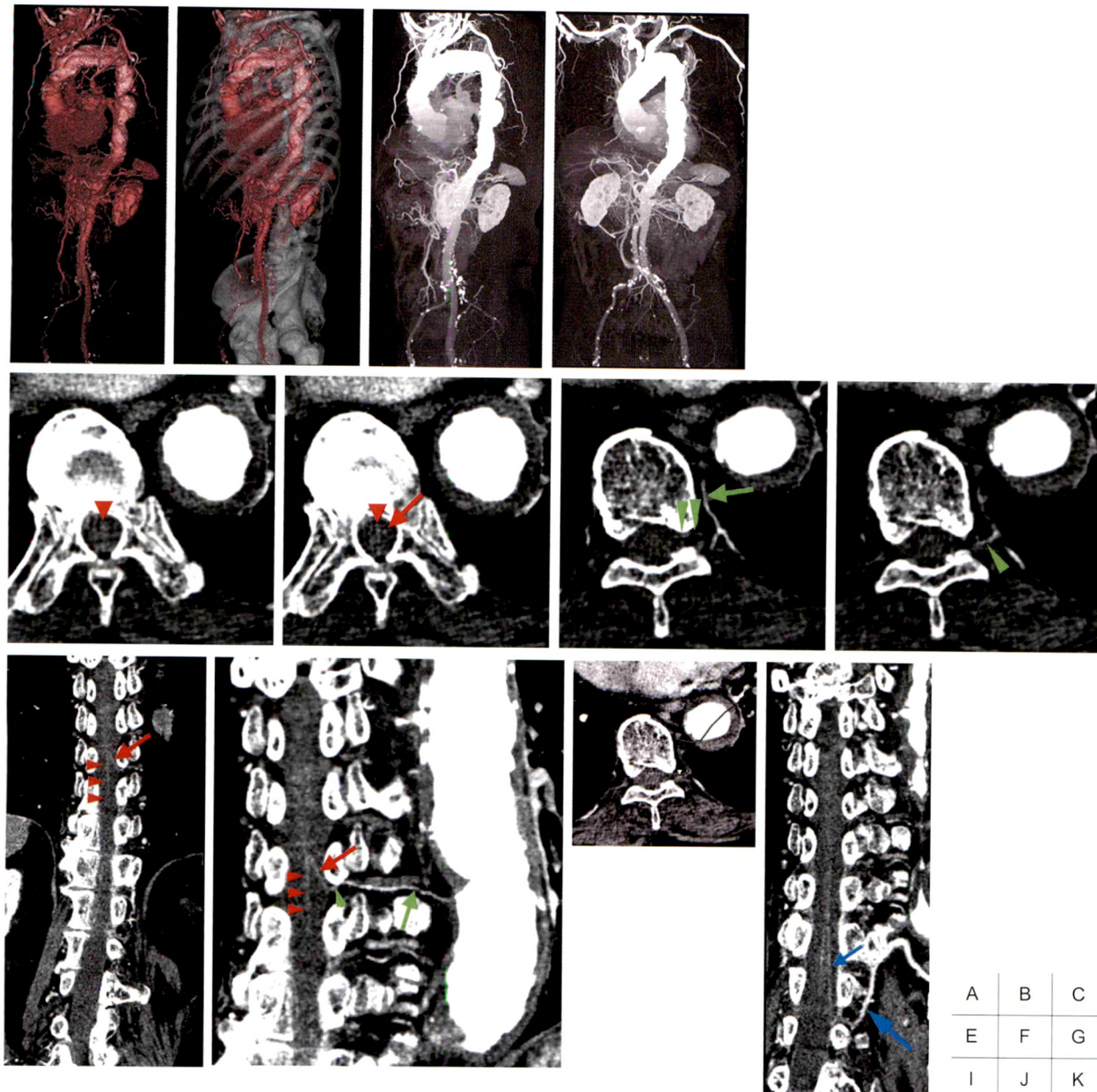


Fig. 2 A male in his 70s with thoracic aortic aneurysm. 16-detector-row MDCT images with 0.5-mm collimation.

A–D: Images of the whole aorta.

A: A VR vascular image with a left anterior oblique view and (B) superimposed bone and vascular images show multiple aortic aneurysms.

C: An MIP image with a left anterior oblique view and (D) antero-posterior view shows stenosis of the right iliac artery.

E–H: Transaxial images with magnified reconstruction.

The anterior spinal artery (red arrowheads) and artery of Adamkiewicz (red arrows) are clearly visualized. Continuity from the stem of the left 9th intercostal artery (green arrow), posterior branch of the intercostal artery (green arrowheads), and the artery of Adamkiewicz through the anterior spinal artery is traceable by paging method observation.

I, J: A curved planar reformation image along the aorta, left 9th intercostal artery, posterior branch of the intercostal artery, and artery of Adamkiewicz through the anterior spinal artery. Reference line is shown in (K).

A patent left 9th intercostal artery is clearly visualized, which supplies the artery of Adamkiewicz that continues to the anterior spinal artery, making a typical hair-pin curve.

L: A curved planar reformation image along the azygos vein, left 1st lumbar vein (large blue arrow), anterior radiculomedullary vein (small blue arrow), and anterior spinal vein.

The anterior radiculomedullary vein can be distinguished from the artery of Adamkiewicz by visualizing its continuity with venous structures, although the anterior radiculomedullary and anterior spinal veins show a similar hair-pin curve.

Adamkiewicz in only 32% of them. In the other 68%, the vessel visualized with timing not allowing venous system visualization was regarded as the artery of Adamkiewicz.¹⁾ From our experience using 16- or 64-detector row CT with 1.0 or 0.5-mm collimation, the artery of Adamkiewicz was visualized in about 90%, which was similar to that using 4-detector row CT, but the continuity between the intervertebral/lumbar artery and artery of Adamkiewicz could be visualized in 90% of them, showing marked improvement. Thus, differentiation between the vein and artery became possible in many cases, but we add contrast-enhanced MRA for patients in whom the visualization of the above continuity is inadequate due to adjacent bone structures. For the clear identification of the artery of Adamkiewicz, it is desirable to use a collimation ≤ 1 mm and a 16- or more detector row scanner. Recent studies have shown an Adamkiewicz artery visualization rate of 83–94% and its increase by improving the contrast enhancement method, reconstruction protocol function, or the intra-arterial contrast agent injection method.^{20–24)}

Case Presentation

Patient with with the aortic arch-descending aortic aneurysm, after Y-graft replacement (**Fig. 2**).

In a male in his 70s, multiple aneurysms were present from the aortic arch to descending aorta on VR images. When original images were observed using the paging method, the anterior spinal artery and artery of Adamkiewicz were identified. A CPR image on the route from the left 9th intervertebral artery to the anterior spinal artery was produced, and the continuity of the aorta, intercostal artery, posterior branch of the intercostal artery, the artery of Adamkiewicz, and anterior spinal artery could be observed on one image. The continuity could be traced even in the area showing passage through the intervertebral foramen. Due to improvement in resolution in the Z-axis direction, the visualization of vascular continuity improved, and the anterior radiculomedullary vein entering the left L1 intercostal vein could be identified in this patient. Entry of this vessel into the azygos venous system confirmed on the CPR image allowed differentiation from arteries.

IMPACT OF THE PREOPERATIVE IDENTIFICATION OF THE ARTERY OF ADAMKIEWICZ ON SURGERY

The successful identification of the intercostal artery that should be reconstructed is beneficial to surgical planning and the operation itself. The usefulness of selective

angiography for preoperatively identifying the artery of Adamkiewicz has also been reported,^{6–9)} but complications often develop. In patients with thoracoabdominal aortic aneurysms or dissection, angiography of the intercostal or lumbar artery itself is almost impossible. There are only a few institutions where the artery of Adamkiewicz is preoperatively identified using angiography. Recent studies have shown noninvasive visualization of the artery of Adamkiewicz using MRI or MDCT,^{1, 2, 25)} and its usefulness for surgery.^{13–17)} The usefulness of the preoperative evaluation of the artery of Adamkiewicz has been re-evaluated.

In the development of postoperative paraplegia, not only the presence or absence of the reconstruction of the artery of Adamkiewicz but also various factors such as the intraoperative arterial cross-clamping time, intraoperative perfusion method, and individual differences in spinal cord hemodynamics may be involved. However, the preoperative clarification of the origin of the artery of Adamkiewicz and reconstruction of only the intercostal/lumbar artery as its supplying blood vessel shorten the intraoperative arterial cross-clamping time,^{13, 15)} and may contribute to the accurate preservation of postoperative blood flow in the artery of Adamkiewicz. If the artery of Adamkiewicz can be confirmed to be located outside the range allowing artery replacement, intercostal artery reconstruction can be omitted, which shortens the operation time.¹⁴⁾ In addition, intraoperative selective perfusion at the level of this artery to minimize intraoperative spinal cord ischemia has been evaluated.¹⁶⁾ When the artery of Adamkiewicz arises from the aortic replacement range, the intercostal artery for reconstruction can be identified before surgery, and the operation time can be shortened compared with the surgical method achieving reconstruction of as many intercostal arteries as possible.^{15, 17)} Since the intraoperative arterial cross-clamping time is associated with postoperative complications, its shortening is a major benefit.

The identification of the artery of Adamkiewicz has the above benefits. A previous study showed a significantly lower complication rate in patients in whom the artery of Adamkiewicz could be preoperatively identified using MRA, and only the intercostal artery at this level was reconstructed in those in whom many intercostal arteries were reconstructed without preoperative identification of this artery in the same institution.¹³⁾

In contrast, Griep et al. ligated intercostal arteries showing no problems under intraoperative monitoring of somatosensory-evoked potentials, and reconstructed

others. As a result, intercostal artery reconstruction was not necessary in any patient. They also reported no spinal cord complications after replacement of less than 10 segments but development of paraplegia in 2 of 21 patients after replacement of 10 segments or more, and an overall incidence of paraplegia of 2%. Based on these results, they speculated that the anterior spinal artery does not depend on the artery of Adamkiewicz alone in terms of hemodynamics.²⁶⁾

The association between the preoperative identification of the artery of Adamkiewicz and surgical results is still controversial. This is partly because only a few years have passed since the establishment of the Adamkiewicz artery evaluation method. Even Griep et al. hoped for the development of a safe preoperative Adamkiewicz artery identification method in the discussion of the above study in 1996.²⁶⁾

In patients with aortic diseases requiring the visualization of the artery of Adamkiewicz, occlusion of the origin of the segmental artery and blood supply to the artery of Adamkiewicz by collateral circulation are often present. Using our simultaneous visualization protocol, collateral circulation between segmental arteries or from the internal thoracic artery can be sometimes visualized using CT, and the blood vessels for reconstruction or preservation can be more accurately determined, which may further improve the surgical results. Recently, in cooperation with the department of cardiovascular surgery, we initiated a method in which vascular reconstruction is performed after functional identification of the vessel most markedly contributing to the blood supply to the spinal cord using intraoperative perfusion cooling of the artery of Adamkiewicz using the supplying vessel suggested by MDCT. No spinal cord complications associated with this method have been observed to the present. Postoperative spinal cord complications cannot be avoided solely by preserving or reconstructing the artery of Adamkiewicz visualized using CT, but may be associated with multiple factors. However, the complication rate can be reduced by identifying the supplying vessel based on morphological information on the artery of Adamkiewicz obtained using MDCT and intraoperative functional examination, and the combined use of intraoperative spinal cord protection methods such as spinal cord drainage and cooling.

Preoperative identification of the artery of Adamkiewicz by imaging has gradually spread since our first report using CT in 2002,¹⁾ and has been included in preoperative evaluation items at many institutions. We expect that its contribution to improvement in surgical

results and methods to avoid postoperative spinal cord complications will be shown by studies in many cases.

REFERENCES

- 1) Takase K, Sawamura Y, Igarashi K, et al. Demonstration of the artery of Adamkiewicz at multi-detector row helical CT. *Radiology* 2002; **223**: 39-45.
- 2) Yoshioka K, Niinuma H, Ohira A, et al. MR angiography and CT angiography of the artery of Adamkiewicz: noninvasive preoperative assessment of thoracoabdominal aortic aneurysm. *Radiographics* 2003; **23**: 1215-25.
- 3) Edited by Takase K, written by Chiba Y and Takase K "Manual for 3-dimensional medical image production - from the basics of Zio M900 to its clinical utilization method -" Medical View -2004.
- 4) Svensson LG, Crawford ES. Cardiovascular and vascular disease of the aorta. Philadelphia: WB Saunders: 1997.
- 5) Svensson LG, Crawford ES, Hess KR, et al. Experience with 1509 patients undergoing thoracoabdominal aortic operations. *J Vasc Surg* 1993; **17**: 357-68, discussion 368-70.
- 6) Koroshetz AM, Taveras JM. Anatomy of the vertebrae and spinal cord. In: Taveras JM, ed. *Radiology: Diagnosis-Imaging-Intervention*. Vol 10, 101 Philadelphia, J. B. Lippincott Company. 1989; 1-14.
- 7) Benson JE, Han JS. Examination of the spine. In: Taveras JM, ed. *Radiology: Diagnosis-Imaging-Intervention*. Vol 10, 102 Philadelphia, J. B. Lippincott Company. 1989; 1-18.
- 8) Wan IY, Angelini GD, Bryan AJ, et al. Prevention of spinal cord ischaemia during descending thoracic and thoracoabdominal aortic surgery. *Eur J Cardiothorac Surg* 2001; **19**: 203-13.
- 9) Williams GM, Perler BA, Burdick JF, et al. Angiographic localization of spinal cord blood supply and its relationship to postoperative paraplegia. *J Vasc Surg* 1991; **13**: 23-33, discussion 33-5.
- 10) Fereshetian A, Kadir S, Kaufman SL, et al. Digital subtraction spinal cord angiography in patients undergoing thoracic aneurysm surgery. *Cardiovasc Intervent Radiol* 1989; **12**: 7-9.
- 11) Savader SJ, Williams GM, Trerotola SO, et al. Preoperative spinal artery localization and its relationship to postoperative neurologic complications. *Radiology* 1993; **189**: 165-71.
- 12) Heinemann MK, Brassel F, Herzog T, et al. The role of spinal angiography in operations on the thoracic aorta: myth or reality? *Ann Thorac Surg* 1998; **65**: 346-51.
- 13) Kawaharada N, Morishita K, Fukada J, et al. Thoracoabdominal or descending aortic aneurysm repair after preoperative demonstration of the Adamkiewicz artery by magnetic resonance angiography. *Eur J Cardiothorac Surg* 2002; **21**: 970-4.
- 14) Fukada J, Morishita K, Hyodoh H, et al. Descending

- or thoracoabdominal aortic aneurysm repair without intercostal vessel reconstruction using contrast magnetic resonance angiography: report of two cases. *Surg Today* 2002; **32**: 163-6.
- 15) Fukada J, Morishita K, Kawaharada N, et al. Less-invasive thoracic aortic aneurysm repair. *Ann Thorac Surg* 2002; **74**: 1244-6.
- 16) Ohtsubo S, Itoh T, Okazaki Y, et al. Selective perfusion of preoperatively identified artery of Adamkiewicz during repair of thoracoabdominal aortic aneurysm. *J Thorac Cardiovasc Surg* 2004; **127**: 272-4.
- 17) Hachiro Y, Kawaharada N, Morishita K, et al. Thoracoabdominal aortic aneurysm repair after detection of the Adamkiewicz artery by magnetic resonance angiography; a way to shorten operating time and improve outcome. *Kyobu Geka* 2004; **57**: 280-3 (in Japanese).
- 18) Koshino T, Murakami G, Morishita K, et al. Does the Adamkiewicz artery originate from the larger segmental arteries? *J Thorac Cardiovasc Surg* 1999; **117**: 898-905.
- 19) Morishita K, Murakami G, Fujisawa Y, et al. Anatomical study of blood supply to the spinal cord. *Ann Thorac Surg* 2003; **76**: 1967-71.
- 20) Backes WH, Nijenhuis RJ, Mess WH, et al. Magnetic resonance angiography of collateral blood supply to spinal cord in thoracic and thoracoabdominal aortic aneurysm patients. *J Vasc Surg* 2008; **48**: 261-71 Epub 2008 Jun 20.
- 21) Nakayama Y, Awai K, Yanaga Y, et al. Optimal contrast medium injection protocols for the depiction of the Adamkiewicz artery using 64-detector CT angiography. *Clin Radiol* 2008; **63**: 880-7 Epub 2008 Apr 14.
- 22) Nojiri J, Matsumoto K, Kato A, et al. The Adamkiewicz artery: demonstration by intra-arterial computed tomographic angiography. *Eur J Cardiothorac Surg* 2007; **31**: 249-55 Epub 2006 Dec 19.
- 23) Takase K, Akasaka J, Sawamura Y, et al. Preoperative MDCT evaluation of the artery of Adamkiewicz and its origin. *J Comput Assist Tomogr* 2006; **30**: 716-22.
- 24) Utsunomiya D, Yamashita Y, Okumura S, et al. 1. Demonstration of the Adamkiewicz artery in patients with descending or thoracoabdominal aortic aneurysm: optimization of contrast-medium application for 64-detector-row CT angiography. *Eur Radiol* 2008; **18**: 2684-90 Epub 2008 May 29.
- 25) Yamada N, Takamiya M, Kuribayashi S, et al. MRA of the Adamkiewicz artery: a preoperative study for thoracic aortic aneurysm. *J Comput Assist Tomogr* 2000; **24**: 362-8.
- 26) Griep RB, Ergin MA, Galla JD, et al. Looking for the artery of Adamkiewicz: a quest to minimize paraplegia after operations for aneurysms of the descending thoracic and thoracoabdominal aorta. *J Thorac Cardiovasc Surg* 1996; **112**: 1202-13, discussion 1213-5.

» Original Article «

Treatment Strategy for Acute Type A Aortic Dissection Complicated with Organ Ischemia

Kazumasa Orihashi, MD, Masamichi Ozawa, MD, Shinya Takahashi, MD, Taiichi Takasaki, MD, Katsutoshi Sato, MD, Tatsuya Kurosaki, MD, Bagus Herlambang, MD, Katsuhiko Imai, MD, and Taijiro Sueda, MD

Objective: We report our current treatment strategy for acute type A aortic dissection with organ ischemia as well as notable findings in our experience.

Materials and Methods: Among 101 cases of acute type A aortic dissection, 25 had organ ischemia. Malperfusion was assessed at the aorta, proximal portion of the branch, organ parenchyma, and organ function by means of multiple modalities, including transesophageal echocardiography (TEE), near-infrared spectroscopy, and physical examinations. It was assessed every time the perfusion status was altered.

Results: There were three operative deaths and one late hospital death. Uncertainty of symptoms and inadequate preoperative assessment in an emergent situation indicated the necessity of an overall check-up of organ ischemia in the operating room on a routine basis. Multi-modality assessment including TEE was helpful for this purpose. Two cases indicated that recovery of a true lumen could be inadequate despite true lumen perfusion including central cannulation. Thrombus in the false lumen appeared to be responsible.

Conclusions: To solve practical problems in treating acute type A dissection with organ ischemia, real-time information on organ perfusion is important for detecting the presence of malperfusion, making an appropriate strategy, and immediately assuring the efficacy of the means taken.

Keywords: aortic dissection, malperfusion, surgery, echocardiography, near-infrared spectroscopy

INTRODUCTION

Aortic rupture and organ ischemia are the two main causes of early death in patients with type A aortic dissection.¹⁻³⁾ The former leads to an unpredictable abrupt onset of circulatory derangement with systemic malperfusion. The latter starts at the onset of dissection or later in the subsequent course and is progressive unless

perfusion is adequately restored. Thus, we have made it a rule to transfer the patient to the operating room even without adequate preoperative assessment in order to avoid irreversible damage of the ischemic organ and/or catastrophe due to aortic rupture before surgery.

Organ ischemia is present in 20% to 40% of cases with acute aortic dissection with various symptoms.⁴⁻⁶⁾ While irreversible organ damage on arrival is beyond the realm of treatment, further progress of ischemic damage should be minimized. Considering the possibility of persistent ischemia despite every effort of restoring perfusion, we have attempted to shed a light on the blind zone during surgery. This paper is aimed to report our current treatment strategies against organ ischemia associated with acute type A aortic dissection, as well as notable findings obtained in our experiences.

Department of Cardiovascular Surgery, Hiroshima University Hospital, Hiroshima, Hiroshima, Japan

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Corresponding author: Kazumasa Orihashi, MD, Department of Surgery II, Kochi Medical School, Kohasu, Oko-cho, Nankoku, Kochi 783-8505, Japan

Tel: +81-88-880-2375, Fax: +81-88-880-2376

E-mail: orihashik@kochi-u.ac.jp

MATERIALS AND METHODS

Between 1997 and 2010, among 101 consecutive cases of acute type A aortic dissection, 25 (24.8%) had associated organ ischemia before surgery. They included 17 male and 8 female patients, 34 to 83 years old (mean age: 62.3 years old). The Ischemic organ included myocardium, brain, upper extremity, spinal cord, intestine, kidney, or lower extremity in 5, 11, 7, 1, 4, 5, and 8 cases, respectively (two, three, or four organs in 7, 3, and 1 case(s), respectively). Eight cases (32%) were hypotensive (<80 mmHg) at arrival due to myocardial ischemia or pericardial tamponade.

The initial diagnosis of aortic dissection and associated complications was made by computed tomography (CT) either in our hospital or in the previous hospital. As long as the diagnosis of the dissection was definite, the patient was immediately transferred to the operating room without an additional CT assessment, even if the image quality was inadequate for us to determine the detailed surgical strategy.

After the induction of anesthesia, transesophageal echocardiography (TEE) was instituted for the preoperative assessment (EUB-555, Hitachi Co, Tokyo, Japan; SSD 5500, Aloka Co., Tokyo, Japan; iE33, Philips Electronics Co., Netherlands) including 1) presence and extent of dissection, 2) presence of rupture to the pericardial and/or pleural space, 3) aortic regurgitation (AR), 4) location of entry, 5) global and regional function of ventricles, and 6) dissection and perfusion in the coronary artery, arch branch arteries and visceral branches.⁷⁻¹⁰ The surgical strategy was finally determined, based on the TEE assessment and preoperative CT findings. In addition, regional oxygen saturation in the bilateral frontal lobes was continuously monitored throughout the surgery with a near-infrared spectroscopy (NIRS) system TOS-96 (TOSTEC Co., Tokyo, Japan).¹¹ When cerebral malperfusion was suspected, orbital Doppler was carried out using a conventional transthoracic echocardiographic probe, which was equipped in the TEE system.¹²

The priority of perfusion was 1) systemic, 2) brain and heart, and 3) intestine and limbs. As long as the patient was hemodynamically stable, an 8-mm ePTFE vascular graft was anastomosed to bilateral axillary arteries with 6-0 polypropylene in an end-to-side fashion. Following median sternotomy, cardiopulmonary bypass was established with the right axillary arterial perfusion and drainage from a two-staged venous cannula. When there was extended dissection or stenosis in the right subclavian

artery, the left axillary artery was used for arterial perfusion. When the patient was in shock status, the femoral artery was cannulated for arterial perfusion to assure the systemic perfusion with minimal delay. In both situations, perfusion in various organs was assessed mainly using TEE, NIRS, and orbital Doppler.¹³ The aorta was repaired under circulatory arrest at the rectal temperature of 25 degrees centigrade and selective cerebral perfusion via the bilateral axillary arteries and a cannula inserted into the left common carotid artery. In case of ischemic limb, the femoral artery was selectively perfused through a cannula which was directed distally.

Figure 1 shows the sites and modalities for assessing the perfusion in each organ. It was checked at one or more sites among 1) the aorta (orifice of branch artery), 2) proximal portion of branch artery, 3) small artery in the parenchyma, or 4) tissue or organ function by means of TEE, NIRS, orbital Doppler, Doppler flowmeter, or physical examination. Perfusion was newly assessed whenever perfusion status was altered, i.e., at the initiation of systemic perfusion and selective perfusion, reperfusion after revascularization, and aortic declamping. If malperfusion was detected, the perfusion routes were changed or added. The efficacy of such strategy was immediately evaluated to avoid an inappropriate navigation.

RESULTS

The surgical procedures for aortic repair were ascending aorta replacement, total arch replacement, or aortic root replacement in 19, 3, and 3 cases, respectively. There were three operative deaths (11.5%) and one late hospital death (3.8%). All of three cases of operative death were in shock status at the start of operation. Among the 11 cases with cerebral ischemia, 5 cases had sustained consciousness disturbance or cerebral infarction, while the remaining 6 cases had no significant sequelae. Several illustrative cases are presented.

A 65 year-old male patient (case #6) with a history of coronary artery bypass grafting (CABG) had a sudden onset of numbness and dull pain in both arms.¹⁴ The CT assessment revealed acute type A dissection with compressed true lumen in the descending to abdominal aorta. Bilateral, radial arteries were hardly palpated. Ultrasonography demonstrated an obstruction in the bilateral axillary arteries (**Fig. 2A**). Blood gas analysis showed metabolic acidosis with base excess level of -10 mEq/L, which was not accountable solely with the upper limb ischemia. Although he had no abdominal pain and

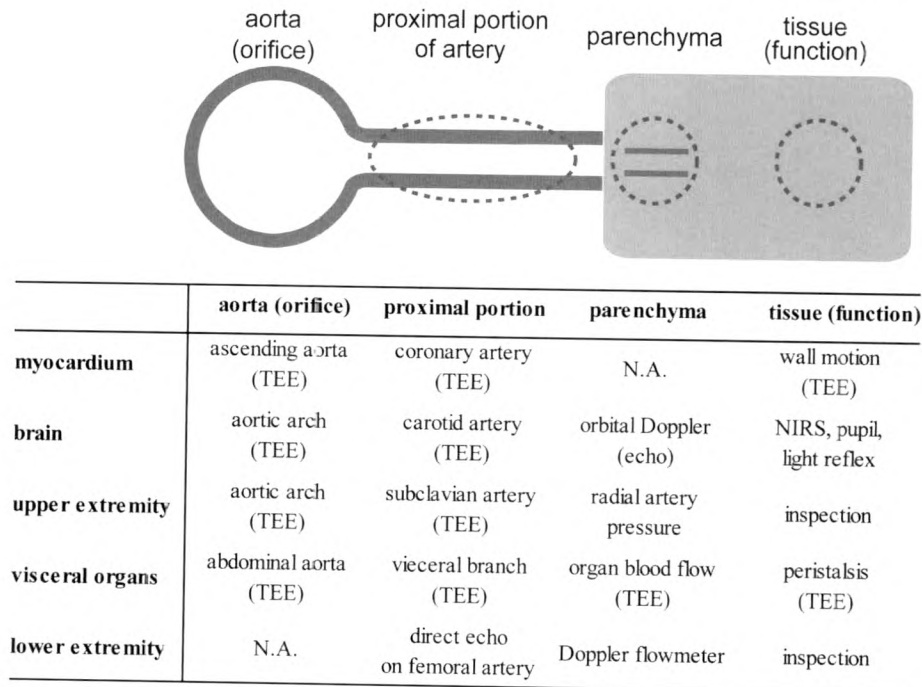


Fig. 1 Sites and modalities for assessing organ malperfusion. Perfusion is assessed at four levels of sites depending on the organ.

N.A.: not applicable; NIRS: near-infrared spectroscopy; TEE: transesophageal echocardiography

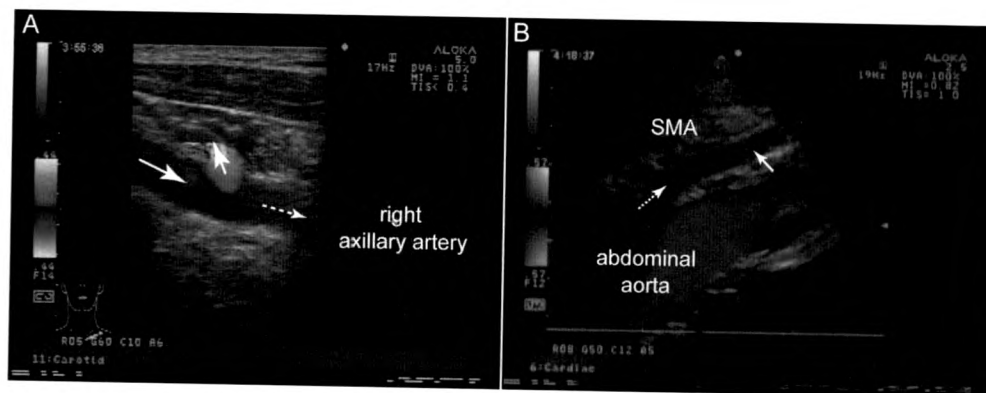


Fig. 2 Preoperative ultrasonograms in case #6. **A:** Occlusion in the right axillary artery. **B:** Obstruction of superior mesenteric artery (SMA). Collateral flow from a branch artery is seen.

the superior mesenteric artery (SMA) was opacified in the CT assessment, the Doppler flow was hardly detectable in the SMA and collateral blood flow into the SMA was detected (**Fig. 2B**). The peristalsis of intestine was very weak although there was no wall thickening or ascites. We concluded that mesenteric ischemia was significant. We had to make a decision to select either of aortic repair or revascularization of SMA and axillary arteries. There was no rupture or malperfusion in other organs at this time. Since he had a history of CABG, aortic rupture was

unlikely to lead to critical pericardial tamponade due to adhesion. A left common iliac to SMA bypass was made with a saphenous vein graft, and the bilateral axillary arteries were fenestrated. The color and peristalsis of the intestine immediately improved, and dull pain in the arm disappeared. The base excess returned to a normal range. Although he developed localized pericardial tamponade with mild hypotension, he underwent aortic repair and had a good postoperative course without complication.

A 57 year-old male patient (case #24) suddenly had

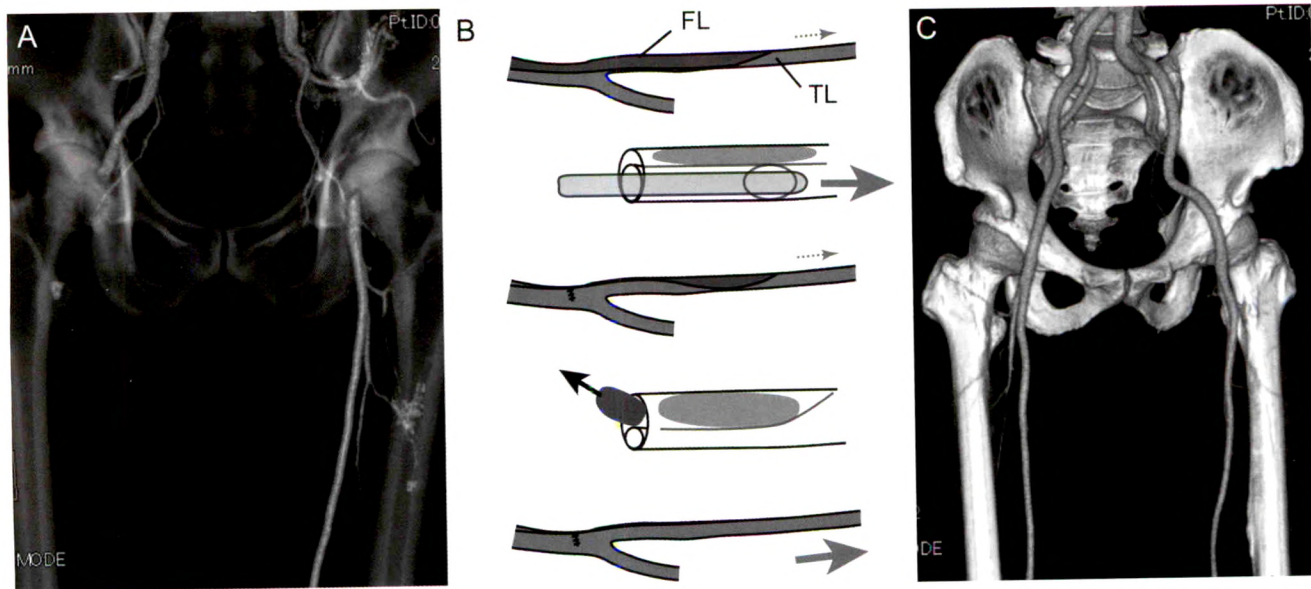


Fig. 3 Computed tomograms (CT) and schematic illustration of mechanism for malperfusion in case #24. **A:** Preoperative CT image with occlusion of right femoral artery. **B:** Mechanism of malperfusion in the right femoral artery. Thrombus in the false lumen (FL) was responsible. True lumen (TL) was compressed. **C:** Postoperative CT image.

lumbago and dull sensation in the legs. CT showed type A dissection with right kidney infarction and obstruction in the right femoral artery (**Fig. 3A**). Although the left external iliac artery was occluded, the left femoral artery was perfused by the collateral circulation from the internal iliac artery. Echocardiography showed moderate to severe AR. Following right axillary artery perfusion, blood flow in the right foot remained undetectable. As we cannulated the right common femoral artery and started selective distal perfusion, blood flow in the right foot became detectable instantaneously. After replacement of the ascending aorta, AR became less than mild. The right femoral artery was transected, and the stump was repaired. However, the blood flow became undetectable again in the right foot and looked pale. Since the limb had been appropriately perfused via a cannula, thrombus in the false lumen near the cannulation site was likely to have collapsed the true lumen (**Fig. 3B**). Thrombus in the false lumen was carefully aspirated by several centimeters. After revision of arterial repair, the foot was well perfused (**Fig. 3C**). Although he developed mild compartment syndrome in the right lower leg and necessitated fascial incision and subsequent skin graft, the leg function fully recovered after several months.

A 54 year-old male patient (case #22) with a history of aortic valve replacement had a sudden onset of weakness in his bilateral legs. The CT assessment revealed type A aortic dissection and total occlusion of the abdominal aorta. Upon

arrival, the anterior to posterior wall of the left ventricle was akinetic. TEE revealed total occlusion in the left coronary ostium and every visceral artery (**Fig. 4A**). In shock status, he was put on bypass with femoral arterial perfusion. The true lumen was soon restored in the aorta, but not in the coronary artery and SMA (**Fig. 4B**). In order to minimize the ischemic time, the aorta was cannulated by Seldinger method under TEE guidance. However, the coronary artery was hardly perfused, and the true lumen in the SMA remained smaller than 50% of the entire lumen (**Fig. 4C**). There was thrombus in the false lumen. After dissection of severe pericardial adhesion, the ascending aorta was replaced. The coronary artery became adequately perfused, and the left ventricle was slightly contracting. However, the true lumen in the SMA remained small (**Fig. 4D**). At this moment, we decided a laparotomy. Although the stomach, liver, jejunum, and sigmoid colon was well perfused, the ileum was necrotic. Unfortunately, the improvement of left ventricular contraction was not adequate, and the patient died the next day.

A 34 year-old female patient (case #25) with Marfan syndrome and a history of type B aortic dissection had a sudden onset of severe abdominal pain with nausea and vomiting. She presented with consciousness disturbance (JCS 30) and left hemiplegia. CT revealed type A aortic dissection without apparent low density area or hemorrhage in the brain. The visceral arteries were opacified. TEE showed mild hypokinesis in the right ventricle, avulsion of right coronary ostium but with detectable

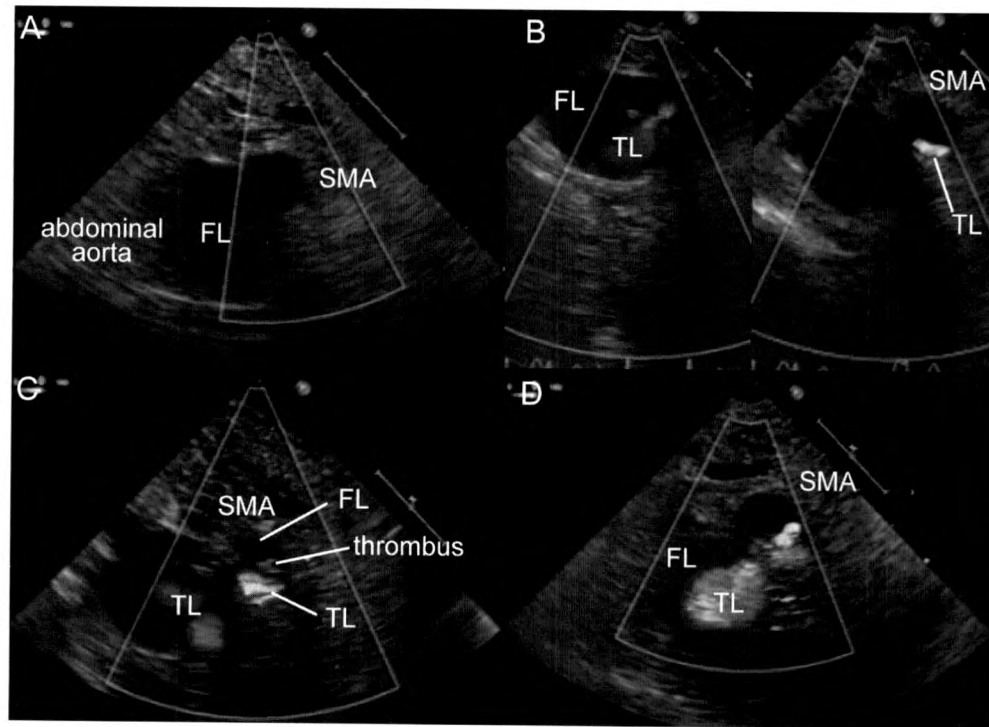


Fig. 4 Transesophageal echocardiograms showing changes of perfusion in superior mesenteric artery (SMA) in case #22. FL: false lumen; TL: true lumen

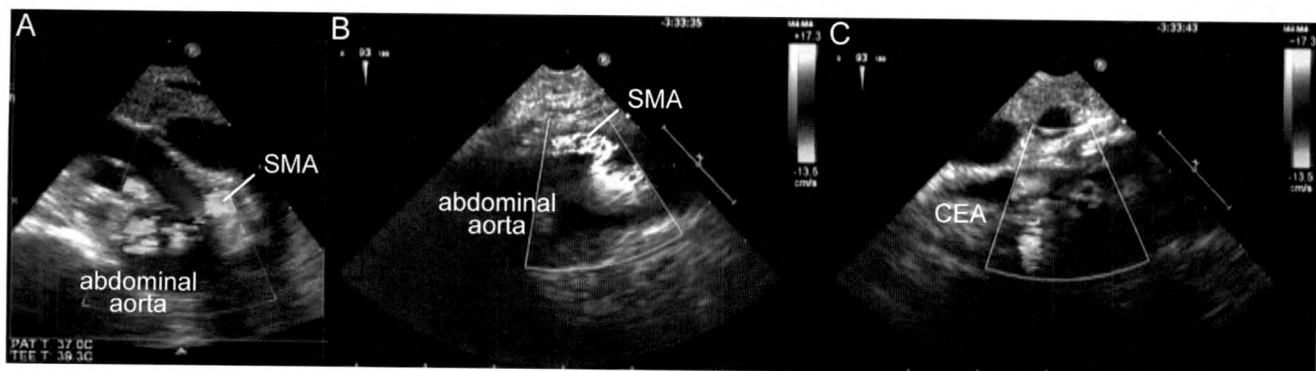


Fig. 5 Transesophageal echocardiograms showing adequate blood flow in visceral arteries in case #25 with abdominal pain. CEA: celiac artery; SMA: superior mesenteric artery

blood flow, moderate AR, narrow true lumen in the right common carotid artery, and patent SMA (**Fig. 5**). Based on these findings, we decided aortic root replacement without a laparotomy. She had good operative course without neurological or abdominal complications.

DISCUSSION

The current study has elucidated the problems in the surgical treatment of acute type A aortic dissection with organ ischemia: 1) fallible symptoms; 2) limited time for

preoperative assessment; and 3) persistent malperfusion despite true lumen perfusion.

Symptoms of patients are often misleading. Case #6 complained of dull pain in the arms but not abdominal pain despite the presence of significant mesenteric ischemia. In case #22, symptoms of myocardial and mesenteric ischemia was masked by the weakness of legs. In contrast, case #25 complained of abdominal pain, but mesenteric ischemia was not present. These results indicate that an overall check-up for organ ischemia during routine care is essential.

However, patients are often hemodynamically unstable, as was noted in 32% of cases in this series due to pericardial tamponade and/or myocardial ischemia. Once a major rupture to the pericardial or pleural space occurs, it becomes extremely difficult to save the life of a patient. Therefore, it is important to put the patient on cardiopulmonary bypass with minimal delay.

In the clinical setting, the quality of CT assessment is often inadequate for making a definite surgical strategy. Thus, we have used intraoperative TEE to obtain the essential information including location of entry, severity of AR, presence of rupture or malperfusion in any organ.⁷⁻¹⁰⁾ In case #25, the absence of mesenteric ischemia was confirmed by CT and TEE despite abdominal pain at the onset, and we could spare time for the laparotomy and concentrate on the aortic repair.

Two cases in this series (case #22 and #24) demonstrated that a recovery of true lumen can be inadequate despite true lumen perfusion. In case #22, malperfusion in the coronary artery and the SMA was persistent despite femoral arterial perfusion and central cannulation, whereas the true lumen in the aorta was immediately restored. This can be a pitfall of central cannulation and suggests the importance of immediate assessment of new perfusion status. The finding in case #24 illustrates the mechanism of persistent malperfusion. The thrombus in the false lumen can interfere with a recovery of true lumen because it occupies space in the vessel and does not dissolve in a short period. However, it is difficult to aspirate the thrombus in the false lumen of SMA or coronary artery during surgery. Bypass surgery or catheter intervention would be a better strategy. While there is always a risk of persistent malperfusion in any organ, it is hardly predictable. It is not practical to set the angiography system ready for every surgical case. A realistic way to detect such an occurrence and make an appropriate decision would be to monitor the perfusion status in each organ at real time by means of modalities listed in **Fig. 1**.

CONCLUSIONS

In acute, type A aortic dissection complicated with organ ischemia, preoperative assessment is often inadequate. Furthermore, malperfusion in the organ can persist despite true lumen perfusion. To solve these problems, real-time information on organ perfusion is important for detecting the presence of malperfusion, making an appropriate strategy, and immediately assuring the efficacy of the means taken.

REFERENCES

- 1) Hagan PG, Nienaber CA, Isselbacher EM, et al. The International Registry of Acute Aortic Dissection (IRAD): new insights into an old disease. *JAMA* 2000; **283**: 897-903.
- 2) von Kodolitsch Y, Schwartz AG, Nienaber CA. Clinical prediction of acute aortic dissection. *Arch Intern Med* 2000; **160**: 2977-82.
- 3) Mehta RH, Suzuki T, Hagan PG, et al. Predicting death in patients with acute type a aortic dissection. *Circulation* 2002; **105**: 200-6.
- 4) Fann JJ, Sarris GE, Mitchell RS, et al. Treatment of patients with aortic dissection presenting with peripheral vascular complications. *Ann Surg* 1990; **212**: 705-13.
- 5) Cambria RP, Brewster DC, Gertler J, et al. Vascular complications associated with spontaneous aortic dissection. *J Vasc Surg* 1988; **7**: 199-209.
- 6) Okita Y, Takamoto S, Ando M, et al. Surgical strategies in managing organ malperfusion as a complication of aortic dissection. *Eur J Cardiothorac Surg* 1995; **9**: 242-6, discussion 247.
- 7) Cambria RP, Brewster DC, Gertler J, et al. Vascular complications associated with spontaneous aortic dissection. *J Vasc Surg* 1988; **7**: 199-209.
- 8) Orihashi K, Matsuura Y, Sueda T, et al. Abdominal aorta and visceral arteries visualized with transesophageal echocardiography during operations on the aorta. *J Thorac Cardiovasc Surg* 1998; **115**: 945-7.
- 9) Orihashi K, Matsuura Y, Sueda T, et al. Aortic arch branches are no longer a blind zone for transesophageal echocardiography: a new eye for aortic surgeons. *J Thorac Cardiovasc Surg* 2000; **120**: 466-72.
- 10) Orihashi K, Sueda T, Okada K, et al. Perioperative diagnosis of mesenteric ischemia in acute aortic dissection by transesophageal echocardiography. *Eur J Cardiothorac Surg* 2005; **28**: 871-6 Epub 2005 Nov 7.
- 11) Orihashi K, Sueda T, Okada K, et al. Near-infrared spectroscopy for monitoring cerebral ischemia during selective cerebral perfusion. *Eur J Cardiothorac Surg* 2004; **26**: 907-11.
- 12) Orihashi K, Matsuura Y, Sueda T, et al. Clinical implication of orbital ultrasound monitoring during selective cerebral perfusion. *Ann Thorac Surg* 2001; **71**: 673-7.
- 13) Orihashi K, Sueda T, Okada K, et al. Detection and monitoring of complications associated with femoral or axillary arterial cannulation for surgical repair of aortic dissection. *J Cardiothorac Vasc Anesth* 2006; **20**: 20-5.
- 14) Chatani N, Orihashi K, Hamamoto M, et al. A case of acute aortic dissection following coronary artery bypass grafting, complicated with upper extremity and bowel ischemia. *Jpn J Cardiovasc Surg* 2005; **34**: 418-21. (in Japanese)

» Original Article «

Cardiac and Aortic Reoperation for Patients with Functional Grafts after CABG

Satoshi Yamashiro, MD, PhD, Yukio Kuniyoshi MD, PhD, Yuya Kise, MD, and Ryoko Arakaki, MD

Objective: Late cardiac and aortic reoperation after CABG is indispensable for patients with atherosclerotic disease, but reoperations are still associated with high morbidity rates.

Patients and methods: Between January 2002 and December 2010, 459 patients underwent coronary artery bypass grafting. Six patients (males; mean age, 65.0 ± 5.7 years) with previous arterial bypass grafts (mean, 2.8 ± 1.2 per patient) required reoperation for cardiac and aortic disease (3, valvular disease; 3, acute type I aortic dissection) during long-term follow-up. The mean interval between the initial operation and reoperation was 5.4 ± 2.0 years. Grafts visualized by preoperative enhanced computed tomography were harvested as pedicles and clamped for myocardial protection. The total arch or ascending aorta was replaced in three patients. The aortic valve was replaced in two patients, and the aortic and mitral valves were replaced in one.

Results: Durations for surgery, total cardiopulmonary bypass, and cardiac ischemia were 611.5 ± 172.6 , 223.2 ± 88.4 , and 133.4 ± 58.0 minutes, respectively. Perioperative myocardial infarction did not develop, and all patients recovered uneventfully with no neurological deficits.

Conclusion: Bypass grafts should be preoperatively visualized and carefully exposed. Cardiac damage must be avoided during reoperation after coronary artery bypass grafting.

Keywords: cardiac reoperation, aortic dissection, coronary artery bypass grafting, internal thoracic artery

INTRODUCTION

The number of patients who have undergone previous coronary artery bypass grafting (CABG) who will require cardiac or aortic reoperations will increase as the population ages.¹⁾ However, treatment presents a complex clinical dilemma, especially for patients with functional grafts after CABG. The region from the internal thoracic (ITA) to the left anterior descending (LAD) artery is routinely used for primary CABG. Specific guidelines

for optimal management of functional ITA grafts at reoperations have not been established. We describe six patients who underwent further surgical procedures for cardiac and aortic disease late after CABG.

PATIENTS AND METHODS

Between January 2002 and December 2010, 459 patients underwent coronary artery bypass grafting at our institution. Six patients (all males; mean age, 65.0 ± 5.7 years) of them required a repeated operation for cardiac and aortic disease after a mean follow-up of 5.4 ± 2.0 years. Two and four patients had undergone on- and off-pump CABG, respectively. The mean number of bypass grafts per patient was 2.8 ± 1.2 . All six had been revascularized with arterial grafts (Table 1). Graft patency was confirmed by post-operative angiography. Three patients were referred to our institution with type A acute aortic dissection.

Thoracic and Cardiovascular Surgery Division, Ryukyu University Hospital, Nishihara, Okinawa, Japan

Received: May 27, 2011; Accepted: August 8, 2011
Correspondence to: Satoshi Yamashiro, MD, PhD. Thoracic and Cardiovascular Surgery Division, Ryukyu University Hospital, 207 Uehara, Nishihara, Okinawa 903-0215, Japan
TEL: +81-98-895-1168; Fax: +81-98-895-1422
E-mail: y3104@med.u-ryukyu.ac.jp

Table 1. Patients' profiles

Case No.	Age	Gender	First procedure	*Interval (y)	Previous bypass	Re-operative procedure
1	65	M	OPCABG	4.2	LITA-LAD	TAR for dissection
2	59	M	On pump CABG	5.8	LITA-LAD (LITA)-RA-LCx12RITA- RCAseg2 RGEA-4PD	Asc. Ao. Replacement for dissection
3	73	M	OPCABG	5.7	LITA-LAD (LITA)-RA-LCx13RITA-RA- LCx12 RGEA-4PD	AVR due to AS
4	64	M	OPCABG	3.3	LITA-LAD (LITA)-RA-LCx12RGEA-4PD	AVR due to AS
5	59	M	OPCABG	4.4	LITA-LAD RGEA-LCx14	Asc. Ao. Replacement for dissection
6	70	M	On pump CABG	9.0	RITA-LAD LITA-RA-LCx12 RGEA-4PD	AVR+MVR due to AS with MR

*Interval between first procedure and repeat operation.

AS: aortic valve stenosis; Asc. Ao.: ascending aorta; AVR: aortic valve replacement; LAD: left anterior descending artery; LCx: left circumflex branch; LITA: left internal thoracic artery; MR: mitral valve regurgitation; MVR: mitral valve replacement; OPCABG: off pump coronary artery bypass grafting; RA: radial artery; RGEA: right gastro-epiploic artery; TAR: total arch replacement; 4PD: posterior descending artery

(LITA)-RA, Y composite graft of radial artery to LITA; LITA-RA, elongation graft of LITA with radial artery (I composite); RITA-RA, elongation graft of RITA with radial artery (I composite)

The other three were admitted due to progressive aortic valve stenosis (AS). Among these, one developed complicated congestive heart failure due to AS with mitral regurgitation (MR). We visualized the previous CABG grafts using enhanced computed tomography (CT). Preoperative enhanced CT upon admission to our hospital visualized bypass grafts in the left (LITA) and right (RITA) internal thoracic arteries as well as the right gastroepiploic artery (RGEA). We usually performed coronary angiography with cardiac catheterization preoperative period except dissection cases.

SURGICAL PROCEDURES

A 5- to 6-cm transverse skin incision was made before the median sternotomy at about 1 cm below the middle and lateral part of the clavicle. Bilateral axillary arteries with or without the right femoral artery (FA) served as the perfusion site for all patients. The right axillary artery

(bilateral axillary arteries, when total arch replacement might be required), the right femoral artery and the right femoral vein were initially exposed to prepare the cardiopulmonary bypass (CPB). After systemic heparinization, an 8-mm-diameter graft was anastomosed to the axillary artery for systemic arterial cannulation and these grafts were used for selective cerebral perfusion (SCP) when dissection was present. The heart, ascending aorta and previous bypass grafts were then exposed through a median sternotomy under CPB assistance if necessary. We then exposed all previous bypass grafts with reference to preoperative CT images using a harmonic scalpel. These grafts could not be recognized by pulsation because of adherence around tissue. Thus, we exposed the previous bypass grafts with surrounding tissue en bloc to avoid damage to the grafts. We clamped the bypass grafts for myocardial protection with intermittent retrograde infused cold blood cardioplegia during the procedure. A left ventricular vent tube was inserted from upper

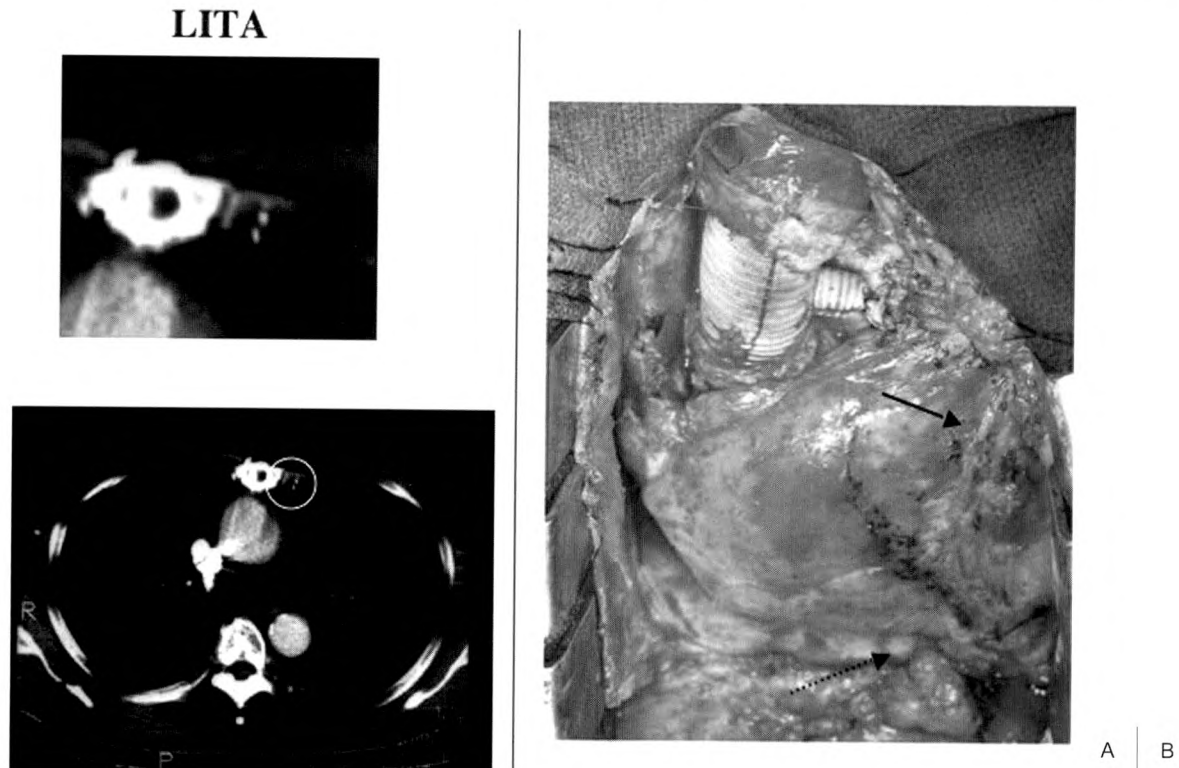


Fig. 1 Computed tomography (CT) images and operative details of Case 5.

- A.** Preoperative enhanced chest CT shows left internal thoracic artery (LITA) tightly attached to chest wall.
- B.** Pedicled LITA (arrow) and right gastroepiploic artery (RGEA) (dotted arrow) are safely exposed and clamped during cardiac arrest.

left pulmonary vein for decompression of left heart as possible. If the patient had a severe adhesion, which makes the procedure difficult to perform, we inserted the LV vent into the pulmonary artery. One patient who underwent LAD revascularization with the RITA at a previous operation required RITA graft translocation as this vessel had crossed over the front of the ascending aorta, rendering an aortotomy for aortic valve replacement (AVR) impossible (Case 6).

The ascending aorta was opened after being clamped immediately below the innominate artery in three patients with a need for valvular replacement. For patients who were to undergo a dissection, their systemic circulation was arrested after the rectal temperature had fallen to 20°C, and then the aorta was opened. Antegrade SCP was established through vascular grafts anastomosed to the axillary arteries, and a perfusion catheter was placed directly into the left carotid and left subclavian arteries. The temperature of the antegrade SCP was maintained at 15°C, and cerebral perfusion was established at a flow

rate of 10–15 mL/kg/min, with a double roller pump that was separate from the systemic circulation. Pressure in the bilateral radial arteries and left carotid artery stump was monitored and controlled between 40 and 50 mmHg by regulating SCP flow.

We replaced the total arch and the ascending aorta in one and two patients with dissection. We believe that distal repair should be sufficiently extended to excise aortic segments containing an intimal tear. One patient received a concomitant femoro-femoral arterial bypass for lower leg ischemia due to dissection. Two of the other three patients underwent AVR and one required AVR with mitral valve replacement (MVR).

CASE FINDINGS

Case 5. Aortic dissection developed in a 59 year-old man 4.4 years after initial OPCABG (LITA to the LAD and RGEA to the left circumflex (LCx) branch). Although preoperative enhanced chest CT revealed that the LITA



Fig. 2 Computed tomography (CT) image of Case 6.

- A.** Preoperative enhanced CT shows right internal thoracic artery (RITA) (arrow), left internal thoracic artery (LITA) (dotted arrow) and right gastroepiploic artery (RGEA) (arrowhead).
B. RITA has crossed over front of ascending aorta (arrow).

(Fig. 1A) appeared tightly attached to the chest wall, we could replace the ascending aorta (Fig. 1B). The pedicled LITA and RGEA were exposed without damage and clamped during cardiac arrest. Post-operative angiography showed that the bypass grafts were well-preserved.

Case 6. A 70 year-old man, who had undergone initial on-pump CABG (RITA-LAD, LITA-LCx branch, RGEA to posterior descending artery), had frequently been admitted for congestive heart failure due to severe AS accompanied by severe MR. Preoperative enhanced CT at the time of admission to our hospital revealed the condition of LITA, RITA and RGEA (Fig. 2A). He had significant left cardiac dysfunction with a 20% ejection fraction. We performed AVR and MVR 9 years after the first CABG. The pedicled LITA and RGEA were exposed without damage and clamped during cardiac arrest. The RITA had crossed over the front of the ascending aorta (Fig. 2B), which obstructed aortic clamping and aortotomy for AVR. Therefore, the RITA was cut and directly anastomosed to the ascending aorta. He required support with intra aortic balloon pumping (IABP) for 2 days after the procedure. Post-operative three-dimensional CT revealed well-preserved bypass grafts including the translocated RITA-LAD (Fig. 3).



Fig. 3 Post-operative computed tomography (CT) image of Case 6. Post-operative three-dimensional CT shows well-preserved bypass grafts including translocated right gastroepiploic artery (RGEA)-LAD (black arrow).

RESULTS

The surgical, total cardiopulmonary bypass and cardiac ischemic durations were 611.5 ± 172.6 , 223.2 ± 88.4 and 133.4 ± 58.0 minutes, respectively. We applied SCP and hypothermic circulatory arrest to three patients

with dissection for 78.2 ± 16.5 and 23.9 ± 38.6 minutes, respectively. Mechanical ventilation was required after surgery for 3.3 ± 3.4 days. Although the durations of surgery and relative CPB were significantly prolonged, all patients recovered uneventfully without neurological deficits or in-hospital death. Perioperative myocardial infarction did not arise, and post-operative CT and/or angiography confirmed that the bypass grafts were well preserved. One patient who underwent AVR with MVR required implantation with a cardioverter defibrillator for ventricular tachycardia and ventricular fibrillation 3 months after the reoperation. With the exclusion of this patient, the mean hospital stay was 41.6 ± 19.6 days.

DISCUSSION

The number of patients requiring further cardiac or aortic surgery after CABG is gradually increasing.¹⁾ However, treatment for such patients presents a complex clinical dilemma, especially for those with functional grafts after CABG.²⁻⁴⁾ The optimal choice of management for cardiac or aortic reoperation after CABG is inconclusive, and reports are sporadic.²⁾ The management of patent arterial grafts including the ITA during repeated cardiovascular surgery after CABG has also been controversial. Reported rates of damage to the conduit in the reoperation range between 5% and 40%.⁵⁻¹¹⁾ Damage to the LITA at reoperation is associated with perioperative mortality rates ranging from 9% to 50%.⁵⁻¹¹⁾ Gillinov and colleagues reported a 5.3% prevalence of damage to ITA grafts, associated with mortality rates of up to 50%.⁶⁾ Therefore, operating under these conditions requires special considerations. Galinanes et al.¹²⁾ do not advocate dissecting or clamping a patent LITA or any other coronary bypass graft during repeated cardiac surgery, or special measures to protect an adequately perfused myocardium. Nevertheless, we believe that a patent graft can compromise myocardial protection owing to enhanced cardioplegia washout resulting from unencumbered flow through the graft. Nakajima et al.¹⁾ established myocardial protection with antegrade cardioplegia and cold blood perfusion of the ITA graft. They described that deep hypothermic SCP also protected the brain and the myocardium supplied by the ITA. However, we suppose that retrograde cardioplegia is useful to establish myocardial protection even at reoperation, especially for patients with severe coronary stenosis. Border zones of the perfused versus the arrested myocardium are, therefore, at potentially high risk for ischemic injury. The goal

of clamping the LITA and the other arterial grafts is to reduce cardioplegia washout and maximize myocardial protection while the heart is arrested.⁵⁾

Late acute type A aortic dissection after CABG is relatively rare, and treatment presents a complex clinical dilemma, especially for patients with a functional graft after CABG. Specific guidelines for optimal management have not been established, and reports have been sporadic. Shinfeld et al.²⁾ found that patients with type A ascending aortic dissection, who had undergone a CABG, have an additional advantage, insofar as their mediastinal adhesions prevent or delay progression of the dissection. Westaby et al.¹²⁾ have achieved a lower mortality rate (6.3%) by applying a conservative method with preservation of the native aortic valve in high-risk patients. We performed emergency surgery for progressive heart failure due to aortic insufficiency in two of our patients and for continuous chest pain in one. Orszulak et al.¹³⁾ commented that delayed aortic dissection after cardiac surgery is not related to technical, operative errors or clamp injury, but to cystic medial necrosis or hypertension. We, therefore, suspect that the main trigger mechanism is not in fact surgical trauma but rather the pathological condition of the aortae of patients indicated for CABG surgery.

In general, three strategies can be recommended for patients with patent ITA grafts.⁹⁾ The more popular technique of clamping both the aorta and the ITA graft has the advantage of shorter CPB times, the application of moderate rather than deep hypothermia and maintenance of a uniformly cooler myocardium than the CPB temperature. However, clamping the ITA has the disadvantage of an inherent risk of ITA damage. The open ITA technique, in which there is no dissection or clamping of the ITA, has the advantages of requiring minimally invasive incisions and avoiding dissection of the ITA pedicle, thus ensuring a shorter operative duration and a decrease in potential risk. A unique feature of this strategy is the temperature difference between the myocardial areas; the myocardium is protected by cardioplegia (4°C) that is cooler than the CPB (20°C), but the ITA territory might approach the temperature of the CPB due to cardioplegia washout.¹⁴⁾ The third strategy involves deep hypothermia and circulatory arrest without ITA or aortic cross clamping, which prolongs an already lengthy procedure.⁹⁾ We believe that to protect the myocardium with cardioplegia is very important. Therefore, we prefer to harvest and clamp arterial grafts in these situations.

Repeated cardiac operations compared with initial

procedures confer an increased risk of damage to the heart, great vessels and, when present, coronary bypass grafts.¹⁵⁾ During repeated procedures, dissection of the mediastinal structures to identify and occlude patent coronary grafts can cause graft damage, typically requiring revision of bypass grafts, which is particularly disadvantageous if arterial grafts have been disrupted. Ismail et al.¹⁶⁾ reported that retrosternal adhesiolysis through an anterior minithoracotomy is a simple and safe approach to facilitate median redo sternotomy that also reduces the risk of associated complications, such as damage to grafts and cardiac structures. We approached a median sternotomy with a left anterolateral thoracotomy in one patient based on this principle. Chest X-rays must be carefully evaluated to establish the course of an ITA graft and its proximity to the chest wall before starting a repeat operation. The arteries of patients who have undergone repeated cardiac and aortic surgery after CABG should be carefully exposed, and damage to bypass grafts should be scrupulously avoided. Computed tomography scanning can evaluate retrosternal distances to structures at risk for injury,¹⁷⁾ and enhanced CT is useful for preoperative visualization of bypass grafts. Three-dimensional CT can clearly delineate the course of revascularized grafts and their proximity to the chest wall.¹⁸⁾ We exposed patent arterial grafts in pedicle form and surrounding tissues without damage in our patients with reference to preoperative CT images. We used the RITA for LAD revascularization in one of our patients because preoperative enhanced CT revealed that the RITA had crossed over the front of the ascending aorta. The RITA was finally cut and directly anastomosed to the ascending aorta. However, the pedicled LITA, as well as the RGEA and RITA, were safely exposed. Previously positioned grafts that cross the midline including the RITA-LAD graft cause more difficulties with accessing the aortic valve via a frontal aortotomy. Okamoto et al.¹⁹⁾ obtained good outcomes using a preserved RITA-LAD graft for aortic valve reoperation. However, we opted to translocate the RITA graft to avoid damage during the procedure. The surgical challenges in these settings are to avoid damaging functional grafts, to secure myocardial protection and accomplish the surgical mission. These conditions require careful operative procedures.

CONCLUSION

Revascularized arteries should be carefully exposed, and damage to bypass grafts should be scrupulously

avoided during repeated cardiac and aortic surgery after CABG. Enhanced CT is useful for the preoperative visualization of bypass grafts.

REFERENCES

- 1) Nakajima M, Tsuchiya K, Naito Y, et al. How to establish myocardial protection during aortic arch operation in patients with patent left internal thoracic artery graft: careful dissection or no touch technique? *J Thorac Cardiovasc Surg* 2002; **124**: 1254-5.
- 2) Shinfeld A, Raanani E. Late acute aortic dissection after coronary artery bypass. *Langenbecks Arch Surg* 2009; **394**: 345-8 Epub 2008 Apr 8.
- 3) Gillinov AM, Lytle BW, Kaplon RJ, et al. Dissection of the ascending aorta after previous cardiac surgery: differences in presentation and management. *J Thorac Cardiovasc Surg* 1999; **117**: 252-60.
- 4) Stanger O, Oberwalder P, Dacar D, et al. Late dissection of the ascending aorta after previous cardiac surgery: risk, presentation and outcome. *Eur J Cardiothorac Surg* 2002; **21**: 453-8.
- 5) Smith RL, Ellman PI, Thompson PW, et al. Do you need to clamp a patent left internal thoracic artery-left anterior descending graft in reoperative cardiac surgery? *Ann Thorac Surg* 2009; **87**: 742-7.
- 6) Gillinov AM, Casselman FP, Lytle BW, et al. Injury to a patent left internal thoracic artery graft at coronary reoperation. *Ann Thorac Surg* 1999; **67**: 382-6.
- 7) Coltharp WH, Decker MD, Lea JW 4th, et al. Internal mammary artery graft at reoperation: risks, benefits, and methods of preservation. *Ann Thorac Surg* 1991; **52**: 225-8, discussion 229.
- 8) Elami A, Laks H, Merin G. Technique for reoperative median sternotomy in the presence of a patent left internal mammary artery graft. *J Card Surg* 1994; **9**: 123-7.
- 9) Byrne JG, Karavas AN, Filsoufi F, et al. Aortic valve surgery after previous coronary artery bypass grafting with functioning internal mammary artery grafts. *Ann Thorac Surg* 2002; **73**: 779-84.
- 10) Lytle BW, McElroy D, McCarthy P, et al. Influence of arterial coronary bypass grafts on the mortality in coronary reoperations. *J Thorac Cardiovasc Surg* 1994; **107**: 675-82, discussion 682-3.
- 11) Dobell AR, Jain AK. Catastrophic hemorrhage during redo sternotomy. *Ann Thorac Surg* 1984; **37**: 273-8.
- 12) Westaby S, Saito S, Katsumata T. Acute type A dissection: conservative methods provide consistently low mortality. *Ann Thorac Surg* 2002; **73**: 707-13.
- 13) Orszulak TA, Pluth JR, Schaff HV, et al. Results of surgical treatment of ascending aortic dissections occurring late after cardiac operation. *J Thorac Cardiovasc Surg* 1982; **83**: 538-45.
- 14) Galiñanes M, Sosnowski A. A patent left internal thoracic artery should not be dissected or clamped during reoperative cardiac surgery. *Ann Thorac Surg*

- 2009; **88**: 1725-6.
- 15) Lotto AA, Owens WA. Intraoperative Doppler velocity measurements to locate patent ITA grafts at reoperation. *Ann Thorac Surg* 2006; **82**: 1108-10.
- 16) Ismail I, Zhang R, Ringe K, et al. Retrosternal adhesiolysis through an anterior minithoracotomy: a novel approach facilitating complete median redo sternotomy with a patent internal thoracic artery graft. *J Thorac Cardiovasc Surg* 2009; **137**: 1034-5 Epub 2008 May 19.
- 17) Cremer J, Teebken OE, Simon A, et al. Thoracic computed tomography prior to redo coronary surgery. *Eur J Cardiothorac Surg* 1998; **13**: 650-4.
- 18) Cohn LH. Myocardial protection for reoperative cardiac surgery in acquired heart disease. *Semin Thorac Cardiovasc Surg* 1993; **5**: 162-7.
- 19) Okamoto H, Tamenishi A, Itoh Y, et al. Aortic valve replacement after midline-crossed internal thoracic artery grafting. *Jpn J Thorac Cardiovasc Surg* 2002; **50**: 435-8.

Impact of Aggressive Decongestion on the Maintenance Phase in Combined Physical Therapy for Lower Extremity Lymphedema

Kotaro Suehiro, MD, Noriyasu Morikage, MD, Osamu Yamashita, MD, Yohikazu Okazaki, MD,
and Kimikazu Hamano, MD

Objectives: To evaluate the impact of initial aggressive decongestion (Phase 1) on the maintenance phase of complex physical therapy (CPT).

Materials and Methods: We reviewed 27 patients with unilateral and 3 patients with bilateral lower extremity lymphedema who started CPT between April, 2009 and October, 2010. Twelve patients elected to undergo in-hospital Phase 1 (Group I), while the other 18 started CPT on an outpatient-basis without having Phase 1 (Group O). The extremity volume was assessed at the beginning of CPT, and then 3 and 6 months later.

Results: A significant reduction in extremity volume was achieved in each group after 6 months of CPT: from 9049 ± 1912 mL at the beginning to 7771 ± 1486 mL ($p = 0.0033$) in group I; and from 7370 ± 1392 mL to 7036 ± 1241 mL ($p = 0.0200$) in group O. However, after 6 months, extremity volume reduction (-845 ± 1283 mL in group I vs. -404 ± 370 mL in group O; $p = 0.7672$) and volume reduction rates ($-23.6 \pm 22.7\%$ in group I vs. $-46.4 \pm 52.2\%$ in group O; $p = 0.2564$) did not differ significantly between the groups.

Conclusion: Phase 1 did not have a significant impact on the maintenance phase in terms of control of the extremity volume for at least 6 months after the induction of CPT.

Keywords: leg, lymphedema, combined physical therapy

INTRODUCTION

Combined physical therapy (CPT) is the mainstay of treatment for extremity lymphedema and generally consists of two phases. Phase 1 is an aggressive decongestion phase which includes skin care; manual lymph drainage (MLD); and a range of motion exercises

and compression, typically applied with multi-layered bandages (MLB), all aimed at maximal decongestion. Phase 2, which is initiated promptly after Phase 1, aims to conserve and optimize the results obtained in Phase 1. It generally consists of compression with a low-stretch elastic stocking, skin care, continued remedial exercise, and repeated self-based MLD as needed.¹⁾ This two-phase treatment has not achieved popularity in Japan; therefore, CPT is induced in various ways. Although patients undergo CPT only on a biweekly- or monthly-basis, they are often well controlled, mainly because successful CPT is dependent on the patients' diligence.^{2, 3)} Thus, we wondered whether Phase 1 treatment is necessary and if so, what is the benefit of Phase 1 treatment? We conducted this study to clarify these points.

Division of Vascular Surgery, Department of Surgery and Clinical Science, Yamaguchi University Graduate School of Medicine, Ube, Yamaguchi, Japan

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Corresponding author: Kotaro Suehiro, MD. Division of Vascular Surgery, Department of Surgery and Clinical Science, Yamaguchi University Graduate School of Medicine, 1-1-1, Minamikogushi, Ube, Yamaguchi 755-8505 Japan
Tel: + 81-836-22-2260, Fax: + 81-836-22-2423
E-mail: ksuehiro-circ@umin.ac.jp

PATIENTS AND METHODS

The subjects of this study were 27 patients with unilateral lymphedema and 3 patients with bilateral lymphedema with minimal symptoms in either leg who commenced CPT at our clinic between April, 2009 and October, 2010. The diagnosis of lymphedema was made by physical examination, and skin ultrasound findings indicating inflammatory changes in the skin and the subcutis, and was finally confirmed by lymphangio-scintigraphy in all patients. Each patient was given an intradermal injection of 111MBq of ^{99m}Tc suspended in 0.1 ml human serum albumin (^{99m}Tc -HSA) into the first interdigital web. When the inguinal nodes and lymphatic trunks in the leg were not visualized within 1 hour from the injection, and/or this was accompanied by congestion of the ^{99m}Tc -HSA in the dermis (dermal back flow sign), it was interpreted as reduced lymphatic function. The choice of inpatient/outpatient, with/without phase 1 was totally dependent on patients' preference. Twelve patients then elected to start Phase 1 treatment on an in-hospital basis (Group I), whereas 18 patients preferred to start CPT on outpatient-basis without undergoing initial aggressive decongestion (Group O). Seven patients in group I and 7 in group O were aged over 70 years old. No patient wished to undergo Phase 1 treatment on an outpatient-basis. The patients in group I were admitted and given daily treatment, including MLD, MLB with low-stretch materials, and exercise by licensed lymphedema therapists and physiotherapists, as described by Földi et al.^{4,5} Toward the end of Phase 1, we instructed patients to care for themselves at home, which included care of the skin and methods of drainage and bandaging. When the extremity volume stabilized, and the patients' self management of their legs was regarded to be sufficient, they were discharged to continue Phase 2 treatments. When complications of CPT developed, the treatment was discontinued immediately, and the patient was referred to specialists. After the complication had resolved, CPT was re-started from the beginning. Patients in group O were instructed in the same self-management methods as group I, at 1–4 week intervals depending on their ability. Although MLD and MLB were provided at each visit, this aimed mainly at demonstrating techniques.

One patient from group I and two patients from group O were excluded from the final analysis. The patient from group I suffered increased seepage from a lymphocele in the scrotum when the leg was wrapped, so his compression therapy was modified to mild below-knee

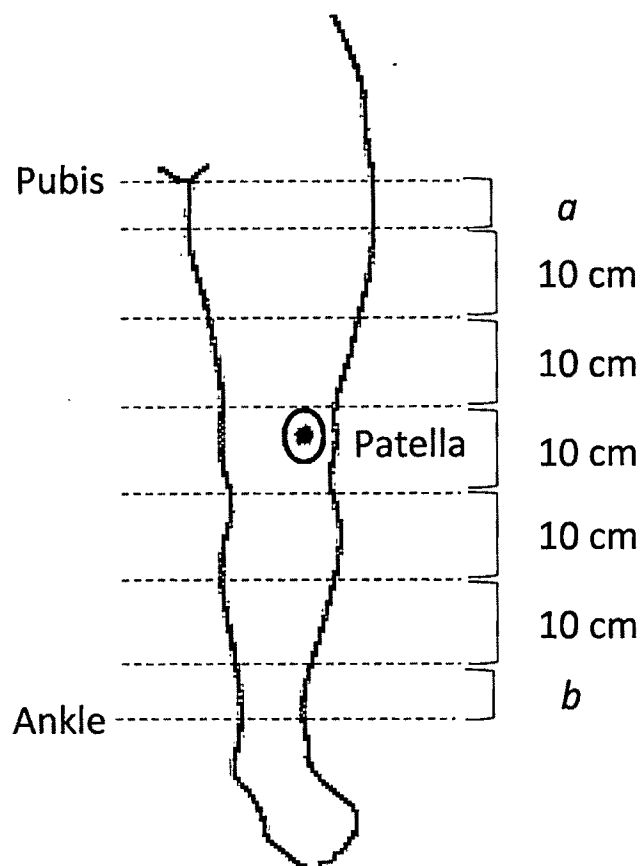


Fig. 1 Points of measurement.

At the upper edge of the patella, circumferences were measured at 10 cm intervals, upward to the level of the pubis, and downward to the ankle. The distances of *a* and *b* were measured separately for calculation. The distances between *a* and *b* were measured separately for calculation.

wrapping, leaving significant amount of edema in the leg intentionally. One patient from group O was not able to continue treatments because of worsening lumbago, and another patient from group O withdrew from the study because of cancer recurrence needing admission. Thus, we assessed 27 patients, 11 patients in group I and 16 patients in group O.

Data collection

Limb measurements were done by the same operator at inclusion, being at the end of Phase 1 in group I, and then 3 and 6 months after the initiation of CPT. The points of measurements are shown in **Fig. 1**. Starting at the upper edge of the patella, At the upper edge of the patella, circumferences were measured at 10 cm intervals, upward to the level of the pubis, and downward to the

Table 1. Patients' characteristics

	Group I (n = 11)		Group O (n = 16)		
Age (years)	74 ± 6		64 ± 13		.0431
Male: Female	2: 9		3: 13		
BMI (kg/m ²)	25.2 ± 3.5		24.1 ± 3.0		N.S.
Initial volume difference between the extremities (ml)	2816 ± 1545		1221 ± 674		.0009
Etiology	0		2		
Primary	11		13		
Secondary	s/p Total hysterectomy		s/p Total hysterectomy		
	+ LN dissection	8	+ LN dissection	8	
	s/p Total hysterectomy		s/p Prostatectomy		
	+ LN dissection		+ LN dissection	2	
	+ irradiation	1	s/p Penile amputation		
	s/p Prostatectomy		+ LN dissection	1	
	+ LN dissection	1	s/p Radical resection for synovial sarcoma	1	
	s/p Inguinal debridement due to trauma		s/p Radical vulvectomy		
	1		+ LN dissection	1	
ISL stage			0		
1	0		15		
2	9		1		
3	2				

ISL: the International Society of Lymphology; s/p: status post-; N.S.: not significant

ankle. The distances of a and b were measured separately for calculation. The volume of the limb was calculated by the following formula for a truncated cone, as described by Casley-Smith⁶⁾:

$$V = h(C^2 + Cc + c^2)/12\pi$$

where V is the volume of an extremity segment, C and c are the circumferences at each end, and h is the distance between the ends. Thus, the extremity volume is the sum of all segment volumes except for the foot.

The actual volume reduction was calculated as; (Extremity volume after treatment)–(Extremity volume before treatment).

The volume reduction rate was calculated as; {(Extremity volume after treatment)–(Extremity volume before treatment)}/{(Extremity volume before treatment)–(Contra-lateral extremity volume)}.

In the patients with bilateral lymphedema, the larger leg was assessed and the other leg was regarded as control.

Statistical analysis

Results are expressed as means ± standard deviation or count (percentage), unless otherwise indicated. The Wilcoxon signed rank sum test was used to determine the significances of the changes in extremity volumes, the actual volume reductions, and the volume reduction rates in each group. The Mann-Whitney U-test was used to compare the above parameters between the groups. Statistical analyses were performed using StatView J-5.0 (SAS Institute, Cary, NC, USA). A *p*-value of less than 0.05 was considered significant.

RESULTS

Table 1 summarizes the patient characteristics of both groups. Patients in group I were older (group I: 74 ± 6 years vs. group O: 64 ± 13 years, *p* = 0.0431) and had larger differences in extremity volume between the legs (group I: 2816 ± 1545 ml vs. group O: 1221 ± 674 ml,

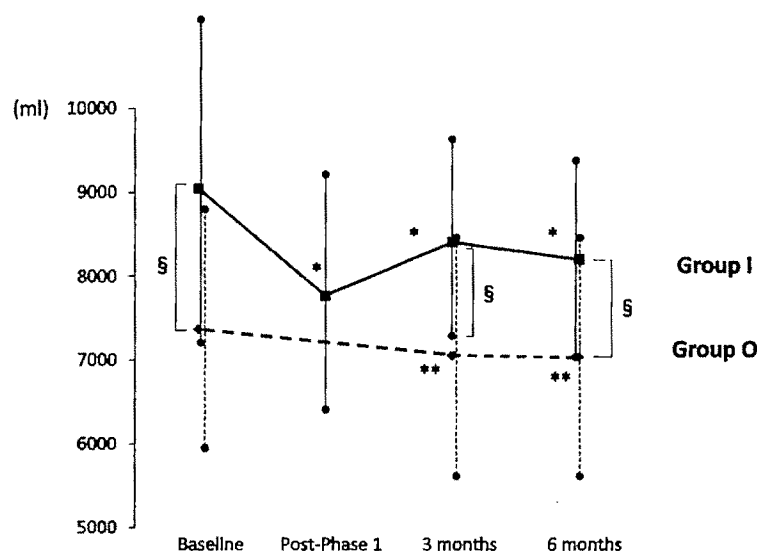


Fig. 2 Changes in extremity volumes.

*: significant versus the value at the beginning of CPT in group I

**: significant versus the value at the beginning of CPT in group O

§: significant between the groups

$p = 0.0009$), while body mass indices were similar (group I: $25.2 \pm 3.5 \text{ kg/m}^2$ vs. group O: $24.1 \pm 3.0 \text{ kg/m}^2$, $p = 0.6761$).

The hospital stay for group I was 10–15 (mean 12) days. One patient suffered an increase in systolic blood pressure to $>200 \text{ mmHg}$ on the first night of Phase 1, but this was settled with adjustment of the bandage pressure. Thereafter, she completed Phase 1 without further problems. Another patient complained of chest discomfort on the first day of Phase 1. Her CPT was discontinued immediately and she was referred to a cardiologist. Although the findings of screening electrocardiogram were within the normal range, she was found to have significant coronary artery stenosis causing angina. After successful coronary intervention, Phase 1 treatment was re-started and completed without problems. There were no reported complications in group O. All of these patients were instructed in the self-management methods over 6–12 (mean 8) weeks.

The changes in extremity volume, actual volume reduction, and volume reduction rates for both groups are shown in Figs. 2–4, respectively. Throughout the study period, affected extremity volume was larger in group I than in group O: at $9049 \pm 1912 \text{ ml}$ vs. $7370 \pm 1392 \text{ ml}$ ($p = 0.0089$) at inclusion, $8413 \pm 1170 \text{ ml}$ vs. $7059 \pm 1321 \text{ ml}$ ($p = 0.0089$) at 3 months, and $8204 \pm 1182 \text{ ml}$ vs. $7036 \pm 1241 \text{ ml}$ ($p = 0.0179$) at 6 months, respectively. In group I, the extremity volume decreased from $9049 \pm$

1912 to $7771 \pm 1486 \text{ ml}$ ($p = 0.0033$) at the end of phase 1, accounting for a $-1278 \pm 873 \text{ ml}$, $-49.5 \pm 26.0\%$ reduction. However, toward the end of 6 months, it increased again to $8204 \pm 1182 \text{ ml}$. This was still a significant reduction ($p = 0.0044$) from the initial volume. In group O, the extremity volume decreased gradually from $7370 \pm 1392 \text{ ml}$ to $7036 \pm 1241 \text{ ml}$ ($p = 0.0200$) over 6 months. The actual volume reduction in group I vs. group O was $-595 \pm 1178 \text{ ml}$ vs. $-382 \pm 383 \text{ ml}$ ($p = 0.7298$) at 3 months and $-845 \pm 1283 \text{ ml}$ vs. $-404 \pm 370 \text{ ml}$ ($p = 0.7672$) at 6 months, respectively. The volume reduction rate in group I vs. group O was $-13.8 \pm 20.4\%$ vs. $-42.5 \pm 42.8\%$ ($p = 0.1671$) at 3 months and $-23.6 \pm 22.7\%$ vs. $-46.4 \pm 52.2\%$ ($p = 0.2564$) at 6 months, respectively. There were no significant differences between the groups. When looking at the individual actual volume reduction, the changes in extremity volume were relatively mild and uniform in group O, whereas they were varied much in group I.

DISCUSSION

The results of this study show that Phase 1 treatment, involving initial aggressive decongestion, does not impact significantly on the maintenance phase, in terms of control of the extremity volume, for at least 6 months after the induction of CPT.

CPT consists of meticulous skin care, MLD, compression therapy, and decongestive exercise therapy. It usually

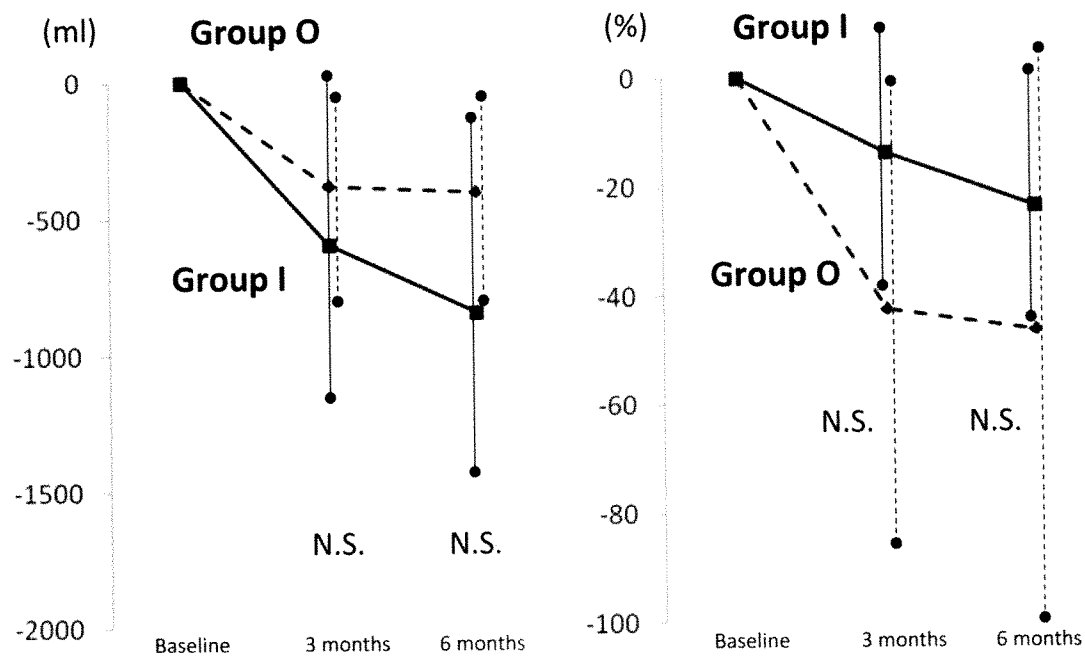


Fig. 3 Changes in actual volume reductions (A) and volume reduction rates (B).
N.S.: not significant

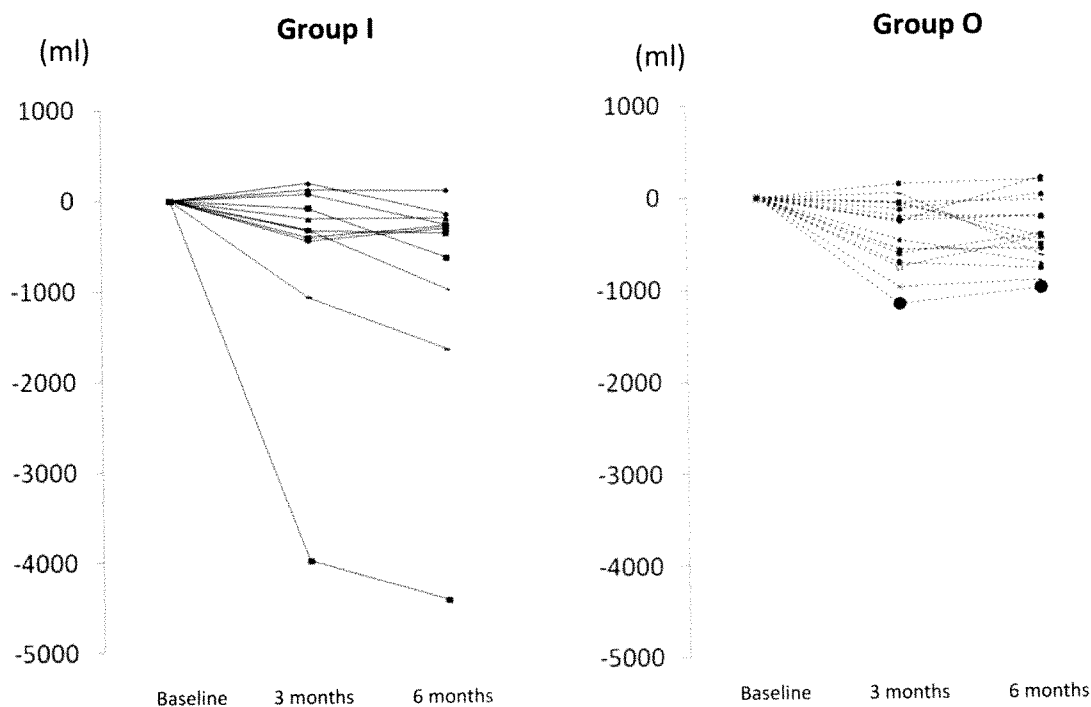


Fig. 4 Individual actual volume reduction.

starts with the decongestion phase (Phase 1), in which MLB and MLD are applied by trained therapists on daily-basis. It aims to drain the pool of protein-hyaluronic acid fluid and maximally restore the extremity volume. This

is followed by Phase 2, in which patients maintain the results of Phase 1 actively, by using elastic compression hosiery and, if necessary, self-based MLD, MLB, and skin care.⁵⁾

The effectiveness of Phase 1 in relieving lower extremity lymphedema has been described, particularly in relation to reducing the extremity volume beyond 6 months from Phase 1.^{3,7-9)} Budger et al. verified the effectiveness of using MLB first, before the wearing of compression hosiery. They found that edema reduction at 24 weeks was better for patients who had used MLB for 18 days, and then wore compression hosiery, than for those who wore only compression hosiery.¹⁰⁾ After an average follow-up of 9 months, Ko et al. also reported that reduced extremity volume was maintained in 82% of patients with lower extremity lymphedema, who were compliant with their treatment.⁹⁾ In the current, retrospective study, since the choice of inpatient/outpatient were totally dependent on patients' preference, the enrollment of the patient was significantly biased. This may be interpreted that older and more diseased patients tended to prefer in-hospital treatments. Taking this biased enrollment into account, we assessed changes in the extremity volume using 3 different parameters, namely the extremity volume, actual volume reduction, and volume reduction rate, and there was no statistical differences between changes in each of the values.

However, this aggressive decongestion phase seems to have distinct advantages. Both the patient and physicians and therapists can recognize and share the best shape of the current extremity at the end of Phase 1, which is a tentative goal of the next step and a strong incentive for the patient. It is thought that 24-hour MLB and daily MLD, including a tissue softening technique, offer the better results. Moreover, patients are often moved deeply by the therapists' diligence during Phase 1, which again inspires the patient to pursue life-long treatment. Phase 1 complications are discovered more easily than those of Phase 2 because Phase 1 is carried out in the hospital, and Phase 2, in the home of the patient. As we reported, aggressive decongestion can cause serious complications, especially at the beginning when a large amount of interstitial fluid shifts into the circulation in a short period. None of the group O patients reported complications, although it is highly likely that we simply were unaware of any. Földi et al. describes the compelling reasons for starting Phase 1 on an in-patient basis as follows: malignant lymphedema, lymphedema of the head and the genitalia, poor general condition with or without serious complications and/or infection, infants, advanced disease such as lymphorrhea, and transportation problems.⁵⁾ All of these criteria are proposed to ensure patients' safety and strictness of treatment, promoting successful CPT.

Two-phase CPT may be ideal, but some patients are too busy to attend to daily treatments or to be admitted, and the others cannot afford the expense. For these patients, we provide advice on self-management techniques, designed according to what they can achieve. Since Phase 1 treatment is performed in few institutes in Japan, the opportunities are limited. We know, however, that many patients are doing well and keeping their extremities in very good shape despite the difficulties. Indeed, the success of CPT depends on patients' diligence. Conversely, non-compliance is associated with a poorer response to CPT.^{3,9)} If the patient does not consistently wear their compression hosiery, relapse is imminent.⁵⁾ and the affected extremities will return to the pre-treatment state within 1 week.⁷⁾

A few of our patients could maintain the minimum extremity volume achieved in the course of Phase 1. This stands to reason since the treatments provided by trained specialists would be surely more effective than self-based management. Unfortunately, there are too few therapists to provide constant support for these patients, and family support is often difficult, which isolates the patient further, and may eventually result in failure of the CPT.

The goal of CPT varies according to each patient's life style and perspectives. Patients with leg lymphedema for decades are often so accustomed to the edema that they are happy with any reduction in swelling; however, they might become noncompliant if the treatment is too much trouble for them. In the present study, 7 of the 12 patients in group I and 7 of the 18 patients in group O were over 70 years. Weak, elderly patients may find it difficult to put on compression tights or bandages on their legs and may feel that the hosiery is burdensome. Moreover, the lower extremity pathophysiology is complicated and multi-factorial, often complicated with functional venous insufficiency, and thus hard to manage.¹¹⁾

Phase 1 treatment seems indicated for patients who accept it and its goals are higher, particularly in terms of extremity volume; however, the absence of Phase 1 is not a failure of CPT, and should be accepted. CPT aims not only to control extremity volume, but it also helps to prevent malignancies, such as angiosarcoma,⁵⁾ and reduce cellulitis.⁹⁾ The patient's ability to incorporate CPT comfortably in their life is the key to them making a life-long commitment. From our perspective, an efficient insurance system for patients and medical staffs, more lymphologists and trained therapists, and adequate information and support are necessary to achieve successful CPT results in Japan.

Since this is a retrospective study of a small number of patients, we cannot make a definite conclusion. However, we do believe that the tendency is similar in every institute, thus justifying the need for a randomized, prospective study. The frequency of cellulitis and malignant formation as well as quality of life should also be assessed in a larger number of patients over a longer period.

CONCLUSION

We conclude that Phase I treatment is effective for reducing the extremity volume, but is not truly necessary to maintain the extremity volume reduced for at least 6 months in the current Japanese situation. For successful CPT, we should endeavor to incorporate it properly for each patient. The overall medical system supporting patients with lymphedema needs to be improved.

REFERENCES

- 1) International Society of Lymphology The diagnosis and treatment of peripheral lymphedema. 2009 Consensus Document of the International Society of Lymphology. *Lymphology* 2009; **42**: 51-60.
- 2) Boris M, Weindorf S, Lasinkski S. Persistence of lymphedema reduction after noninvasive complex lymphedema therapy. *Oncology (Williston Park)* 1997; **11**: 99-109; discussion 110, 113-4.
- 3) Hinrichs CS, Gibbs JF, Driscoll D, et al. The effectiveness of complete decongestive physiotherapy for the treatment of lymphedema following groin dissection for melanoma. *J Surg Oncol* 2004; **85**: 187-92.
- 4) Foldi M. Treatment of lymphedema. *Lymphology* 1994; **27**: 1-5.
- 5) Foldi M, Foldi E. Foldi's textbook of lymphology: Elsevier; 2006.
- 6) Casley-Smith JR. Measuring and representing peripheral oedema and its alterations. *Lymphology* 1994; **27**: 56-70.
- 7) Yamamoto R, Yamamoto T. Effectiveness of the treatment-phase of two-phase complex decongestive physiotherapy for the treatment of extremity lymphedema. *Int J Clin Oncol* 2007; **12**: 463-8 Epub 2007 Dec 21.
- 8) Yamamoto T, Todo Y, Kaneuchi M, et al. Study of edema reduction patterns during the treatment phase of complex decongestive physiotherapy for extremity lymphedema. *Lymphology* 2008; **41**: 80-6.
- 9) Ko DS, Lerner R, Klose G, et al. Effective treatment of lymphedema of the extremities. *Arch Surg* 1998; **133**: 452-8.
- 10) Badger CM, Peacock JL, Mortimer PS. A randomized, controlled, parallel-group clinical trial comparing multilayer bandaging followed by hosiery versus hosiery alone in the treatment of patients with lymphedema of the limb. *Cancer* 2000; **88**: 2832-7.
- 11) Suehiro K, Furutani A, Morikage N, et al. Routine diagnostic venous ultrasound and LAS for leg edema of unknown cause. *Ann Vasc Dis* 2010; **3**: 222-7.

Open Repair of Infra Renal Abdominal Aortic Aneurysms: A Single Center Experience from the Developing World

Nalaka Gunawansa, MBBS, MD, Thushan Goonerathne, Rezni Cassim, and Mandika Wijeyaratne

Introduction: In the absence of endovascular aneurysm repair due to financial constraints, Abdominal Aortic Aneurysm (AAA) in Sri Lanka is managed exclusively by open surgery. We report our experience with open AAA repair with emphasis on peri-operative morbidity and mortality.

Methods: Seventy nine consecutive open AAA repairs were carried out between April 2004 and March 2010. A multiple regression model was used to identify predictors of significant peri-operative morbidity and mortality.

Results: Mean age of the study cohort was 68 years. There were 63 (80%) males and 16 (20%) females. Mean aneurysm diameter was 6.4 (3.5–9.70) cm. Twenty seven (34%) underwent emergency surgical repair (group-1) while 52 (66%) had elective repair (group-2).

The peri-operative mortality was 10/27 (37%) in group-1, 4/52 (7.6%) in group-2, ($p = 0.0035$). Significant post-operative morbidity was seen in 5/17 (29%) in group-1 and 7/48 (15%) in group-2, ($p = 0.27$). Aneurysm diameter >7 cm ($p = 0.001$), emergency repair ($p = 0.004$), history of smoking ($p = 0.002$), aortic cross-clamp time >60 minutes ($p = 0.044$), and need for post-operative ventilation >24 hours ($p = 0.024$) were found to be independent predictors of peri-operative mortality or significant morbidity.

Conclusion: Open aneurysm repair still has a strong place especially in the limited resource setting, with acceptable outcomes.

Keywords: open aortic aneurysm repair, peri-operative morbidity and mortality, limited resource setting

INTRODUCTION

The peri-operative morbidity and mortality of open Abdominal Aortic Aneurysm (AAA) repair varies widely among different centers, depending on case volume and surgical expertise. Most 'high volume' centers report an operative mortality rate of less than 5% for elective repair and 30%–50% for emergency repair.^{1–3} There is also a severe dearth of published data on the operative outcomes of AAA in the developing world with limited resources.

We, in the University Surgical Unit at the National Hospital of Sri Lanka (NHSL), are one of just three special-

ized vascular units in the country serving a population of 20 million. All three units function at the NHSL, which is the largest tertiary care hospital in the country situated in the capital Colombo, with a bed-strength of over 4000. There is approximately equal distribution of cases among the units with an annual case volume of 15–20 each. This is a government sponsored national health care system with free health care for all. Even for the limited number of patients seeking private health care, costs of endovascular stenting are prohibitive. Hence, the management of AAAs in Sri Lanka is exclusively by open repair. We report our experience with open AAA repair in the era of endovascular stenting, with emphasis on peri-operative morbidity and mortality.

METHOD

We performed a retrospective analysis of prospectively collected data on all AAA referred to our unit between April 2004 and March 2010. The primary prospective database was supplemented by information retrieved from individual case notes and clinic records. An AAA

*Department of Vascular Surgery and Organ Transplantation,
National Hospital of Sri Lanka, Colombo, Sri Lanka*

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Corresponding author: Nalaka Gunawansa, MBBS, MD.

Department of Vascular Surgery and Organ Transplantation,
National Hospital of Sri Lanka, Kynsey road, Colombo 8,
Colombo, Sri Lanka

Tel: +94-773737644, Fax: +94-112691111

E-mail: nalakagunawansa@yahoo.co.uk

was defined as a focal dilatation of the infra-diaphragmatic aorta with a maximal diameter of over 3 cm on cross sectional imaging with Computerized Tomography (CT) scan. All thoraco-abdominal, supra-renal and isolated iliac aneurysms were excluded from the study.

All patients with clinically apparent or suspected aneurysm rupture were offered surgical repair on an emergency basis. Among those who had no evidence of rupture, all symptomatic AAAs, mycotic aneurysms and asymptomatic aneurysms with a maximal diameter of over 5.5 cm on CT were offered elective surgical repair. Those who declined surgery, or were found to be poor surgical candidates with an unacceptable mortality risk due to overwhelming comorbidities (American Society of Anesthesiologists physical status classification; ASA P4 or worse) were managed conservatively. Those who had asymptomatic AAA with a maximum diameter of <5.5 cm were entered in to a conservative management program with risk factor modifications. This latter group was followed up at six monthly intervals with abdominal ultrasonography to monitor aneurysm expansion. Those who developed 'new' symptoms, attributable to the aneurysm or had an aneurysm expansion rate of >0.5 cm per six months, were offered elective surgical repair.

All open AAA repairs were preferentially carried out via a midline trans-peritoneal approach. Polyester (Dacron) grafts were used in 14 mm and 16 mm sizes depending on the healthy native aortic diameter. The graft morphology (tube versus bifurcated) was dependent on the extent of the aneurysm. Accordingly, simple aortic end to end repair was carried out in aneurysms confined to the aorta with a favorable common ostium at the iliac bifurcation while aorto-iliac or aorto-femoral end to side repairs were carried out for aneurysms extending in to the iliac arteries. The immediate post-operative care was in the surgical Intensive Care Unit (ICU) with selective ventilation. Subsequent care was in the general surgical ward. Following discharge, all patients were followed up as outpatients at approximately 2–4 week intervals for the first 3 months. The long-term follow up was either at the NHSL or the regional hospital of the patient's choice.

All patients who underwent open aneurysm repair were studied further to identify possible markers of peri-operative morbidity and mortality. The variables studied were gender (male, female), age (<70, ≥70), history of smoking (yes, no), diabetes (yes, no), history of coronary artery disease; CAD (yes, no), preoperative renal impairment (Serum creatinine <120 μmol/L, ≥120 μmol/L), maximum aneurysm diameter on CT (<7 cm, ≥7 cm), nature of the surgery (elective, emergency), aortic cross-clamp time

(<60 mins, ≥60 mins), operative blood loss (<1 L, ≥1L), and need for post-operative ventilation (<24 hours, ≥24 hours). In-hospital mortality and post-operative morbidity (day 0–30) was assessed using the Clavien-Dindo (CD) classification system for surgical complications.⁴⁾ Accordingly, In-hospital mortality (CD grade V) was taken as the primary end point while significant post-operative morbidity requiring surgical, radiological or endoscopic intervention (CD grade III) or life threatening organ dysfunction (CD grade IV) were taken as secondary end points.

Categorical variables were summarized with frequencies and percentages. Continuous variables were summarized with the mean ± standard deviation. Univariate analysis was performed using Spearman's rank correlation in the case of continuous variables and Wilcoxon rank-sum tests in the case of binary variables. Multiple logistic regression analysis was used to identify risk factors for significant post-operative morbidity and peri-operative mortality. Statistical analysis was performed using SPSS (version 15.1) software.

RESULTS

A total of 141 successive patients with infra-renal AAA were managed in our unit during the study period. The demographic and baseline characteristics of the patient population are shown in **Table 1**. Among them, 33 (23%) had clinical evidence of aneurysm rupture on the first assessment. Six of these patients who were in profound shock succumbed prior to reaching the operating room while the remaining 27 (Group 1) underwent emergency surgical repair. One hundred and eight patients (77%) had no clinical evidence of aneurysm rupture and were managed electively. Among them, 32 (23%) were found to have asymptomatic AAA with a maximum diameter of <5.5 cm on CT scan. These patients were managed with risk factor modifications and ultra sound surveillance at six monthly intervals. Seventeen (12%) such patients have subsequently been lost to follow up while 7 developed 'new' symptoms or were found to have significant aneurysm expansion and were operated on an elective basis. Of the remaining 8 patients, 4 have died due to unrelated causes while the other 4 continue to be on the surveillance program.

Seventy six (54%) of the patients managed electively were either symptomatic or had a maximal aneurysm diameter of >5.5 cm and were considered for elective surgical repair. Twelve such patients declined surgical intervention while 19 were found to have unacceptable peri-operative mortality risk (vide infra) and were managed conservatively.

Table 1 Baseline characteristics of the patient population (n = 141)

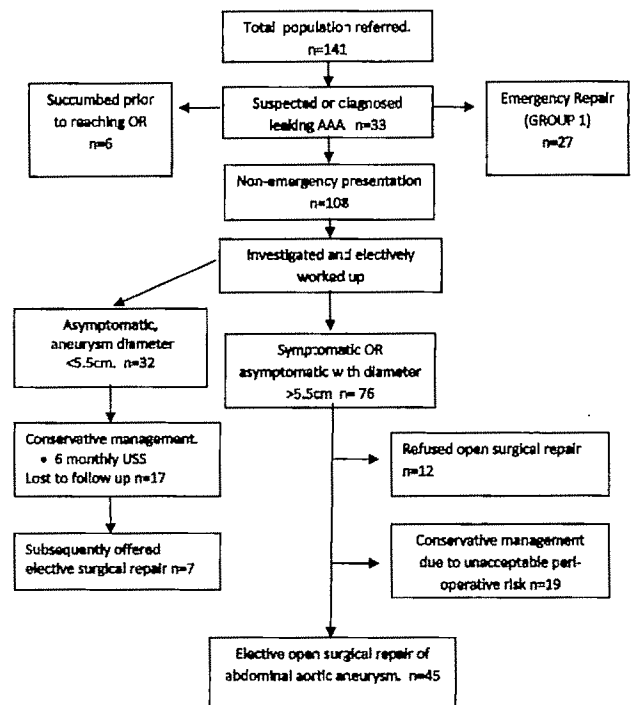
Variable	n	%
Age		
≥70 years	77	55
<70 years	64	45
Gender		
Male	122	87
Female	19	13
Presentation		
Elective	108	77
Emergency	33	23
Co-existing conditions		
Coronary artery disease	66	47
Diabetes mellitus	30	21
Chronic obstructive pulmonary disease	41	29
Impaired renal function	29	21
History of smoking	98	70
Hypertension	54	38

The remaining 45 patients underwent elective AAA repair. Along with the 7 patients who were operated while on surveillance, the total number of elective surgical repairs was 52 (Group 2). **Figure 1** summarizes the management of all AAA referred to our unit in the period studied. Demographic and baseline characteristics of the surgically repaired AAA (Group 1 & 2) are shown in **Table 2**.

The primary reasons for patients being considered as having unacceptable peri-operative mortality risk for elective aneurysm repair were significant cardiac disease (congestive cardiac failure, unstable angina, recent myocardial infarction within 3 months or poor cardiac functional status), 15; severe Chronic Obstructive Pulmonary Disease (COPD) with poor lung function tests, 6; and chronic kidney disease stage IV or V with serum creatinine of >200 µmol/L, 7. Nine patients had more than one of the above risk factors.

The mean age of those who underwent surgical repair was 68 years (range 35–86). Sixty three (80%) were male while the remaining 16 (20%) were female. The maximal aneurysm diameter among this group ranged from 3.5–9.7 cm with a mean of 6.4 cm. There were three aneurysms operated with a maximal diameter of less than 5.5 (3.5, 4.1 and 4.2) cm due to clinical and radiological evidence of infection. All three presented with a history of fever, leukocytosis, elevated inflammatory markers and a saccular aneurysm on imaging. Infection in the aneurysm wall was proven by microbiological cultures from intra-operative samples taken in two of these aneurysms (*Klebsiella* species and *mycobacterium tuberculosis*), while the third failed to show any significant microbial growth in culture despite strong clinical suspicion. The clinical presentation at the time of being considered for surgical repair is summarized in **Table 3**.

The mean operative time in group 1 was 4.7 hours

**Fig. 1** The breakdown of 141 patients with infra-renal AAA managed by our unit from April 2004–March 2010.**Table 2** Baseline characteristics of patients who underwent open surgical repair (n = 79)

Variable	n	%
Age	68.3 ± 5.8	
≥70 years	44	56
<70 years	35	44
Gender		
Male	63	80
Female	16	20
Presentation		
Elective	52	66
Emergency	27	34
Co-existing conditions		
Coronary artery disease	40	51
Diabetes mellitus	9	11
Chronic obstructive pulmonary disease	29	37
Impaired renal function	16	20
History of smoking	47	59
Hypertension	22	28
Aneurysm diameter	6.4 ± 0.7	
<5.5 cm	15	19
5.5–7 cm	30	38
≥7 cm	34	43

(range 3–6 hours) compared to 4.3 hours (range 3–7 hours) in group 2 ($p > 0.05$). The operative time was calculated as total 'in room' time spent in the operating theatre. The duration of post-operative ventilation was significantly different between the two groups, with 22/27 (80%) of group 1 being ventilated for more than 24 hours compared to 28/52 (54%) of group 2 ($p < 0.01$). The mean duration of ICU stay was 4 (range 1–8) days and 2 days (range 1–5) for groups 1 and 2 respectively, ($p < 0.01$).

Table 3 Clinical presentation of the repaired AAA n = 79

Presentation		n	%
Asymptomatic; diameter >	Diameter ≥ 5.5 cm	21	27
Asymptomatic; with	Expansion >0.5 cm/6months	1	1
	Abdominal pain +/-back pain	17	22
Symptomatic	Back pain alone	10	13
	Claudication / distal gangrene	3	4
	Abdominal pain/ back pain	14	18
Rupture/ Leaking n = 27	collapse	12	15
	Primary aorto-intestinal fistula	1	1

Table 4 Basic comparison of ruptured AAA repaired on an emergency basis (Group 1) and non-ruptured AAA repaired electively (Group 2)

Variable	Group 1 (n = 27)	Group 2 (n = 52)	p value
Operative time	3.7 hrs (2–6)	3.5 hrs (2–7)	p >0.05
Post-op ventilation beyond 24 hrs	22/27 (80%)	28/52 (54%)	p <0.01
Post-op ICU stay	4d (1–8)	2d (1–5)	p <0.01
In-hospital mortality	10/27 (37%)	4/52 (7.6%)	p <0.05
Post-operative morbidity	5/17 (29%)	7/48 (15%)	p >0.05

Table 4 summarizes the findings in groups 1 and 2.

The in-hospital mortality was 10/27 (37%) in group 1 and 4/52 (7.6%) in group 2, ($p = 0.0035$). Among the 10 deaths in group 1, 6 died per-operatively due to massive hemodynamic disturbances and blood loss. The remaining 4 died while in the ICU due to myocardial ischaemia (2) and multi organ dysfunction (2). The causes of death in group 2 were myocardial ischaemia (2), acute bilateral subdural hemorrhage (1) and multi organ dysfunction (1). Significant post-operative morbidity was seen in 5/17 (29%) of group 1 and 7/48 (15%) of Group 2, ($p = 0.27$). The significant morbidities included myocardial ischaemia (5), pneumonia (5), acute kidney injury (3), acute lower limb ischaemia (3), colonic ischaemia (2) and burst abdomen (1). All three patients with acute kidney injury required temporary dialysis and recovered completely between 14–25 days. Two patients with acute limb ischaemia were successfully treated by embolectomy and fasciotomy respectively while the third patient required a below knee amputation. One patient with colonic ischaemia required laparotomy and colonic resection while the other who had mild ischaemic colitis responded to conservative management.

Multivariate analysis of risk factors (**Table 5**) showed an aneurysm diameter ≥ 7 cm ($p = 0.005$), emergency surgical repair ($p = 0.011$), aortic cross-clamp time ≥ 60 minutes ($p = 0.034$), and the need for post-operative ventilation ≥ 24 hours ($p = 0.021$), as independent predictors of in-hospital mortality and significant post-operative morbidity. Other variables studied including age, gender, history of smoking, diabetes, hypertension, renal insufficiency and operative blood loss did not show statistical significance.

DISCUSSION

This is an audit of 141 consecutive AAA managed in our unit during a period of 6 years. Our indications for surgical intervention were in accordance with internationally accepted protocols and recommendations.^{5–8} Approximately one quarter of the AAA referred during the study period had clinical or radiological evidence of aneurysm rupture at first presentation. The in-hospital mortality for emergency repair of ruptured AAA was 37%. In addition, non-fatal significant post-operative morbidities were encountered in 29%. Among those who underwent elective surgical repair, the in-hospital mortality and significant post-operative morbidity rates were 7.6% and 15% respectively.

The reported incidence of peri-operative adverse events in open AAA repair varies widely in the literature. A meta-analysis of the reported literature showed a 30-day operative mortality rate for elective infra-renal AAA repair ranging between 1.4% and 6.5%.⁹ For ruptured AAA, the reported mortality rate ranges between 23% and 69%.^{2, 9, 10} While certain high-volume centers of excellence report very low mortality rates (from 0% to 1.2%),^{3, 11, 12} multi-institutional nationwide data continue to show significantly higher incidence of mortality ranging between 4.2% and 8.4%.^{11, 12} This discrepancy has been seen as a result of the case volume related difference in outcome. Many reports have identified a strong relationship between the operative outcome and case volume of the individual surgeon or the institution. Birkmeyer and colleagues^{13, 14} reported elective AAA repair mortality rate of 7.8% for low volume centers (<17 /year), as opposed to 4.9% in high volume (>79 /year) centers. Our own elective aneurysm repair mortality rate

Table 5 Multivariate analysis of risk factors for peri-operative adverse events

Variables		Total AAA repairs (N)	Operative mortality and morbidity n (%)	Univariate analysis p	Multivariate analysis OR (95% CI) p	
Gender;	Male	63	18 (29)	0.63	0.06–5.14	0.62
	Female	16	8 (50)			
Age;	≥70y	44	15 (34)	0.85	0.12–4.22	0.71
	<70y	35	11 (31)			
History of smoking ;	Yes	47	20 (43)	0.12	0.86–49.08	0.07
	No	32	06 (19)			
Diabetes;	Yes	09	04 (44)	0.45	0.21–54.72	0.39
	No	70	22 (31)			
CAD;	Yes	40	13 (33)	0.90	0.2–5.27	0.98
	No	39	13 (33)			
COPD;	Yes	29	9 (31)	1.0	0.85–1.92	0.87
	No	50	17 (34)			
Renal insuff.;	Yes	16	06 (38)	0.52	0.011–2.26	0.18
	No	63	20 (32)			
AAA diameter ;	≥7 cm	34	20 (59)	0.002	2.43–136.4	0.005
	<7 cm	45	06 (13)			
Surgery;	Emergency	27	18 (67)	0.007	1.75–77.77	0.011
	Elective	52	08 (15)			
Aortic cross clamp;	≥60 mins	36	21 (58)	0.02	1.16–42.03	0.034
	<60 mins	43	05 (12)			
Operative blood loss;	≥1 L	23	07 (30)	0.07	0.03–1.3	0.09
	<1 L	56	19 (34)			
Perop. blood transfusion;	Yes	61	17 (28)	0.09	0.07–2.39	0.13
	No	18	09 (50)			
Periop. Myocardial isch.;	Yes	9	9 (100)	0.011	0.01–1.1	0.017
	No	70	17 (24)			
Postop ventil.;	≥24 hrs	31	19 (61)	0.014	1.35–38.25	0.02
	<24 hrs	48	07 (15)			

CAD: coronary artery disease; COPD: chronic obstructive airway disease

of 7.6% with a case volume of 15–20 per year compares favorably with these findings.

Despite many recent advances in surgical and anesthetic peri-operative management, the operative mortality after open repair of ruptured AAA has remained fairly constant. A meta-analysis by Hoornweg and colleagues¹⁵⁾ in 2008 which included over 100 studies and approximately 60000 patients with ruptured aneurysms showed an overall mortality rate of 48.5% for open repair. This high mortality rate is probably related to factors such as delay in recognition and intervention, extreme hemodynamic instability, profound blood loss and suboptimal peri-operative care in the emergency setting.^{16, 17)} The situation is no different in Sri Lanka where all suspected ruptured AAAs are referred and transferred to the NHSL for definitive care. The average travel time for transfers is around 6 hours with distances that may exceed 250 km. Further, there is very limited critical care support during transfer with only basic support available in the ambulance systems. In addition, many such patients initially present to and are investigated in non-specialized units prior to vascular surgical referral causing considerable delay in definitive intervention. Furthermore, the logistical difficulty in obtaining emergency access to the operating theatre confounds the problem.

Despite being the largest tertiary hospital in the country, there is no dedicated operating facility for vascular surgical emergencies. A single 'casualty' operating room is shared among all general surgical emergencies including vascular emergencies. There is limited intensive care back up with only 8 ventilator beds available for elective and emergency surgical admissions. Despite a falsely reassuring 37% mortality for operated ruptured AAA compared to the international figures, the overall mortality for all ruptured aneurysms referred to our unit during this period is 48.5% (16/33).

Various factors have been reported as predictive factors for peri-operative adverse events after elective open AAA repair. These include advanced age, large aneurysm diameter, pre-operative renal dysfunction, history of smoking, COPD, CAD, prolonged aortic cross-clamp time, greater operative blood loss and intra-operative myocardial ischaemia.^{6, 18–21)} While COPD and intra-operative myocardial ischaemia were not studied separately, we did not find gender, age, pre-operative renal dysfunction, diabetes and CAD to be independently predictive of peri-operative adverse events in our study population. History of smoking and greater operative blood loss showed a positive association with morbidity and mortality, albeit not statistically significant. However,

aneurysm diameter ≥ 7 cm, emergency surgical repair, aortic cross-clamp time ≥ 60 minutes and the need for post-operative ventilation ≥ 24 hours were found to be independent predictors of in-hospital mortality and significant post-operative morbidity.

One limitation in the present study is its retrospective nature. However, with a comprehensive prospective data base maintained since 2002, supplemented by retrieved individual case records, we believe that the data included in the study was complete and representative with minimal bias. Another possible limitation is that we have not considered aneurysm morphology (saccular or fusiform), possible infective or inflammatory aetiology, COPD and intra-operative myocardial ischaemia as separate variables in our analysis. Aggressive investigation of all patients with cardiac enzyme assays was also not carried out in the absence of clinical justification. In addition, even though operative blood loss was considered in the analysis, we have not considered the transfusion needs or its effects.

In conclusion, the management of AAA in Sri Lanka at present is almost exclusively by open surgical repair. Ours unit is one of only three specialized units in the country managing AAA with approximately equal distribution of cases numbering 15–20 per year. A collective nationwide audit has not been possible as there were no published records from the other centers up to the time of writing. Our observed operative mortality and morbidity rates for open repair of infra-renal AAA compare favorably with the reported figures in the literature for both ruptured as well as non-ruptured aneurysms.

REFERENCES

- 1) Heller JA, Weinberg A, Arons R, et al. Two decades of abdominal aortic aneurysm repair: have we made any progress? *J Vasc Surg* 2000; **32**: 1091-100.
- 2) Verhoeven EL, Kapma MR, Groen H, et al. Mortality of ruptured abdominal aortic aneurysm treated with open or endovascular repair. *J Vasc Surg* 2008; **48**: 1396-400 Epub 2008 Oct 1.
- 3) Hertzer NR, Mascha EJ, Karafa MT, et al. Open infrarenal abdominal aortic aneurysm repair: the Cleveland Clinic experience from 1989 to 1998. *J Vasc Surg* 2002; **35**: 1145-54.
- 4) Clavien PA, Barkun J, de Oliveira ML, et al. The Clavien-Dindo classification of surgical complications: five-year experience. *Ann Surg* 2009; **250**: 187-96.
- 5) Katz DA, Littenberg B, Cronenwett JL. Management of small abdominal aortic aneurysms. Early surgery vs watchful waiting. *JAMA* 1992; **268**: 2678-86.
- 6) Brewster DC, Cronenwett JL, Hallett JW Jr, et al. Guidelines for the treatment of abdominal aortic aneurysms. Report of a subcommittee of the Joint Council of the American Association for Vascular Surgery and Society for Vascular Surgery. *J Vasc Surg* 2003; **37**: 1106-17.
- 7) Eliason JL, Clouse WD. Current management of infrarenal abdominal aortic aneurysms. *Surg Clin North Am* 2007; **87**: 1017-33 viii.
- 8) Chaikof EL, Brewster DC, Dalman RL, et al. The care of patients with an abdominal aortic aneurysm: the Society for Vascular Surgery practice guidelines. *J Vasc Surg* 2009; **50**: S2-49.
- 9) Hallin A, Bergqvist D, Holmberg L. Literature review of surgical management of abdominal aortic aneurysm. *Eur J Vasc Endovasc Surg* 2001; **22**: 197-204.
- 10) Schermerhorn ML, O'Malley AJ, Jhaveri A, et al. Endovascular vs. open repair of abdominal aortic aneurysms in the Medicare population. *N Engl J Med* 2008; **358**: 464-74.
- 11) Lawrence PF, Gazak C, Bhirangi L, et al. The epidemiology of surgically repaired aneurysms in the United States. *J Vasc Surg* 1999; **30**: 632-40.
- 12) Dimick JB, Cowan JA Jr, Stanley JC, et al. Surgeon specialty and provider volumes are related to outcome of intact abdominal aortic aneurysm repair in the United States. *J Vasc Surg* 2003; **38**: 739-44.
- 13) Birkmeyer JD, Siewers AE, Finlayson EV, et al. Hospital volume and surgical mortality in the United States. *N Engl J Med* 2002; **346**: 1128-37.
- 14) Birkmeyer JD, Stukel TA, Siewers AE, et al. Surgeon volume and operative mortality in the United States. *N Engl J Med* 2003; **349**: 2117-27.
- 15) Hoornweg LL, Storm-Versloot MN, Ubbink DT, et al. Meta analysis on mortality of ruptured abdominal aortic aneurysms. *Eur J Vasc Endovasc Surg* 2008; **35**: 558-70 Epub 2008 Jan 15.
- 16) Bown MJ, Sutton AJ, Bell PR, et al. A meta-analysis of 50 years of ruptured abdominal aortic aneurysm repair. *Br J Surg* 2002; **89**: 714-30.
- 17) Kantonen I, Lepäntalo M, Brommels M, et al. Mortality in ruptured abdominal aortic aneurysms. The Finnvasc Study Group. *Eur J Vasc Endovasc Surg* 1999; **17**: 208-12.
- 18) Bauer EP, Redaelli C, von Segesser LK, et al. Ruptured abdominal aortic aneurysms: predictors for early complications and death. *Surgery* 1993; **114**: 31-5.
- 19) Sasaki S, Takigami K, Kuniyama T, et al. Abdominal aortic aneurysms in aged patients: analysis of risk factors in non-ruptured cases. *J Cardiovasc Surg (Torino)* 1999; **40**: 1-5.
- 20) Berry AJ, Smith RB 3rd, Weintraub WS, et al. Age versus comorbidities as risk factors for complications after elective abdominal aortic reconstructive surgery. *J Vasc Surg* 2001; **33**: 345-52.
- 21) Roger VL, Ballard DJ, Hallett JW Jr, et al. Influence of coronary artery disease on morbidity and mortality after abdominal aortic aneurysmectomy: a population-based study, 1971–1987. *J Am Coll Cardiol* 1989; **14**: 1245-52.

Early and Long-term Effects of the Autologous Peripheral Stem Cell Implantation for Critical Limb Ischemia

Takahiro Nishida, MD,¹ Yasutaka Ueno, MD,² Takashi Kimura, MD,² Ryousuke Ogawa, MD,² Kunihiro Joo, MD,¹ and Ryuji Tominaga, MD¹

Objective: Therapeutic angiogenesis by peripheral blood mononuclear cells (PB-MNCs) implantation has been shown to be a safe and effective treating for critical limb ischemia (CLI). We herein report our investigation of the long-term efficacy of implantation of granulocyte-colony stimulating factor (G-CSF)-induced PB-MNCs to treat patients with CLI for which surgical bypass and/or percutaneous transluminal angioplasty are not possible.

Methods and Methods: Eleven cases were enrolled in this study. Following an injection of G-CSF (250 ug/day) for 3 days, PB-MNCs ($1.1 \pm 0.5 \times 10^{10}$ including $1.5 \pm 0.2 \times 10^7$ CD34-positive cells) were harvested by apheresis and then injected into 13 ischemic limbs.

Results: Resting pain either diminished or improved in 10 cases (91%) at 4 weeks, and ulcer formation was cured in 6 out of 10 limbs (60%) after treatment. The time required to enhance the arteries at the level of foot-joint by angiography which was performed in the abdominal aorta was shortened by 1 month (10 ± 4 seconds) and 6 months (12 ± 1) compared with the pretreatment time (15 ± 5). Three patients died after treatment, and the actuarial survival rate at 3 years was 73%. Freedom from major amputation at 3 years was 92%.

Conclusion: The local injection of G-CSF-induced PB-MNCs showed striking early and long-term effects.

Keywords: peripheral blood mononuclear cells, arteriosclerosis obliterans, thromboangiitis obliterans, critical limb ischemia, angiogenesis

INTRODUCTION

Critical limb ischemia (CLI) due to arteriosclerosis obliterans (ASO) or thromboangiitis obliterans (TAO) is a disease that significantly decreases a patients' quality of life because of leg pain, ulceration, and gangrene.

¹Department of Cardiovascular Surgery, Kyushu University, Fukuoka, Fukuoka, Japan

²Department of Cardiovascular Surgery, Shimonoseki City Hospital, Shimonoseki, Yamaguchi, Japan

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Corresponding author: Takahiro Nishida, MD. Department of Cardiovascular Surgery, Kyushu University Graduate School of Medical Sciences, 3-1-1 Maidashi, Higashi-ku, Fukuoka, Fukuoka 812-8582, Japan

Tel: +81-92-642-5557, Fax: +81-92-642-5566

E-mail: tnishida@heart.med.kyushu-u.ac.jp

Although several therapies, including medical and surgical procedures, may reduce patients' symptoms and improve the condition of their legs, a lot of patients are not candidates for surgery or percutaneous transluminal angioplasty, and 25% of CLI patients requires a major amputation of a leg within 1 year after the first diagnosis of CLI.¹⁾ Recently, a new therapy using bone marrow mononuclear cells (BM-MNCs) has been developed to treat CLI, and the implantation of granulocyte-stimulation factor (G-CSF)-derived peripheral blood mononuclear cells (PB-MNCs) into the ischemic limb have also been shown to be effective.²⁻⁴⁾ However, a few reports⁵⁾ of critical limb ischemia have, so far, examined the long-term (>3 years) effect of PB-MNCs therapy for CLI. We herein report the acute and long-term effects of PB-MNCs therapy against CLI.

Table 1 Profiles of the patients underwent PB-MNCs therapy

Case	Gender	Age	Rest pain	Ulcer	DM	HD	Diagnosis
1 (L)	Male	75	+	–	+	+	ASO
2 (L)	Female	72	+	+	+	–	ASO
3 (R)	Male	69	+	+	+	+	DM
3 (L)	Male	69	+	+	+	+	DM
4 (L)	Male	70	+	+	+	–	ASO
5 (L)	Male	79	+	+	–	–	ASO
6 (R)	Female	83	+	+	+	+	ASO
7 (L)	Male	74	+	–	–	–	ASO
8 (R)	Female	82	+	+	–	–	ASO
9 (R)	Female	81	+	+	+	–	TAO
9 (L)	Female	81	+	+	+	–	TAO
10 (L)	Male	69	+	–	–	–	ASO
11 (R)	Female	83	+	+	–	–	ASO

L: left lower limb; R: right lower limb; HD: hemodialysis; DM: diabetes mellitus; ASO: arteriosclerosis obliterans; TAO: thromboangiitis obliterans

MATERIALS AND METHODS

Patients with CLI suffering from rest pain and/or ulcer formation on the limbs for at least three months, which did not improve despite possible bypass graft operation and/or medical treatment, were included in this study. All patients underwent angiography before this treatment, and 2 radiologists and 3 vascular surgeons evaluated whether PTA and/or bypass grafting was possible. When it was determined that it was impossible to perform PTA and/or bypass grafting, we then considered PB-MNCs therapy. Patients with severe ischemic heart disease, cerebrovascular disease, proliferative diabetic retinopathy, malignancy within one year, or who were unable to give fully informed consent, were excluded. After approval by the medical ethics committee of Shimonoseki City Hospital, 11 patients (13 legs) underwent the PB-MNCs therapy during from December 2006 to May 2008. All patients underwent angiography before and after PB-MNCs therapy. Two radiologists carried out the angiographic examination of the lower body from the brachial artery and injected contrast medium into the abdominal aorta near the bifurcation. We measured the time from the injection of the contrast medium to the starting point of the enhancement of the artery at the level of the foot-joint. Characteristics of the patients are shown in **Table 1**. All patients were suffering from rest pain, and ulcer formation with and without gangrene were

recognized in 10 legs of 8 patients. Six patients were suffering from diabetes mellitus (DM) and 3 patients underwent hemodialysis for chronic renal failure. Nine patients were suffering from arteriosclerosis obliterans (ASO), and the rest was suffering from DM angiopathy (case 3) or thromboangiitis obliterans (TAO; case 9). Previous treatments for patients are listed in the **Table 2**. All patients underwent medical treatment at least 3 months before PB-MNCs therapy. Two patients had already undergone major amputation in the contra-lateral limb. Patients with diabetic angiopathy and TAO and one patient with ASO had only been treated medically before PB-MNCs therapy. The rest of the ASO patients had undergone PTA and/or bypass surgery before PB-MNCs therapy.

PROTOCOL FOR PB-MNCs THERAPY

Patients were injected with 250 µg of G-CSF subcutaneously for 3 days, and the next day PB-MNCs were harvested by cell apheresis using a cell separator (COBE Spectra™, GAMBRO BCT, Lakewood, USA), in a final suspension volume of approximately 50 ml. We harvested $1.1 \pm 0.5 \times 10^{10}$ total mononuclear cells, of which $1.4 \pm 0.5 \times 10^7$ were CD 34 positive cells. Within a few minutes after harvesting PB-MNCs, the collected stem cell suspension was divided into 0.5 ml with a syringe and injected with a 26 gauge needle into 40–60 points of the

Table 2 Previous treatments of the patients underwent PB-MNCs therapy

Case	Previous treatment
1	PTA to Lt. EIA. Graft replacement of Lt. EIA and Rt. FA.
2	PTA and Bilateral FPAK bypass (twice). Amputation of the contra-lateral limb.
3	Medication
4	Lt. FPBK bypass. Amputation of the contra-lateral limb.
5	PTA to Rt. CIA and EIA
6	PTA to bilateral CIA and CFA
7	FF bypass
8	Resection of the gangrene of the Lt. 2nd finger.
9	Medication
10	Lt. FPBK bypass. PTA to Lt. ATA.
11	Medication

PTA: percutaneous transluminal angioplasty; EIA: external iliac artery; FA: femoral artery; FPAK: femoro-popliteal above knee; FPBK: femoro-popliteal below knee; CIA: common iliac artery; CFA: common femoral artery; FF: femoro-femoral; ATA: anterior-tibial artery

Table 3 Results of ulcer after PB-MNCs therapy

Case	Gender	Age	Ulcer	No. Size (mm)	Improvement	Recurrence
2 (L)	Female	72	+	2 (22 × 20, 12 × 8)	+	—
3 (R)	Male	69	+	2 (18 × 10, 10 × 8)	+	—
3 (L)	Male	69	+	1 (8 × 8)	+	—
4 (L)	Male	70	+	1 (5 × 5)	+	—
5 (L)	Male	79	+	1 (5 × 3)	—	—
6 (R)	Female	83	+	1 (8 × 5)	+	+
8 (R)	Female	82	+	1 (5 × 5)	—	—
9 (R)	Female	81	+	1 (8 × 5)	+	—
9 (L)	Female	81	+	1 (10 × 5)	+	—
11 (R)	Female	83	+	1 (5 × 5)	+	+

L: left lower limb; R: right lower limb; No.: number

ischemic limb under venous anesthesia using midazolam (0.5 mg/kg). All patients were discharged from our hospital on the fifth day.

RESULTS

There were no significant side effects of this procedure during the five days of hospitalization. Ten (91%) of 11 patients reported either diminished or deceased rest pain at 2 weeks after PB-MNCs therapy. **Table 3** shows the number, size and fate of the ulcers after treatment. Ulcer formation was completely cured or improved in 8 (80%)

out of 10 legs at 4 weeks after PB-MNCs therapy, while no improvement of ulcer formation was observed in the other 2 cases during the follow-up period. Recurrences of ulcers were observed in 2 patients (**Table 3**). Thus, 60% of ulcers were cured without recurrence after PB-MNCs therapy. **Figure 1** shows an improvement of an ischemic ulcer in one patient (case 2 in **Table 1**). One patient died of pneumonia at 3 months after PB-MNCs therapy. This patient underwent a major amputation, 1 month after PB-MNCs therapy.

The ankle-brachial index (ABI) was improved from a baseline of 0.77 ± 0.21 to 0.91 ± 0.27 and 0.99 ± 0.1 at 1



Fig. 1 Ulcer formation in case 2 (A) was completely healed after PB-MNCs therapy (B).

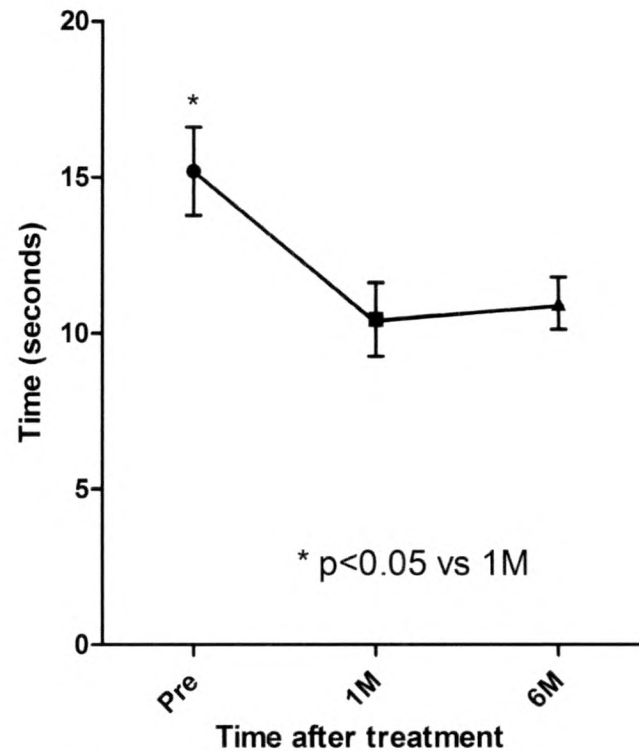


Fig. 2 The time required to enhance the arteries by angiography at the level of the foot-joint was significantly shortened at 1 month (10 ± 4 seconds, $p < 0.05$) after PB-MNCs therapy compared with the time of pretreatment (15 ± 5).

and 2 months after PB-MNCs therapy, respectively, and the ABI was still higher one (0.84 ± 0.28) and two years (0.90 ± 0.13) later. The time required to enhance the arteries at the level of the foot-joint by angiography was significantly shortened at 1 month (10 ± 4 seconds, $p < 0.05$) and 6 months (12 ± 1) after PB-MNCs therapy compared with the time of before treatment (15 ± 5 , **Fig. 2**).

The actuarial survival rate and freedom from major amputation of the lower limb at 36 months after PB-MNCs therapy were 73% and 92%, respectively (**Fig. 3**). The causes of death were a hepatic coma and sepsis in 2 patients (cases 1 and 6) and pneumonia (case 7) in 1 patient. Because no severe infection was observed in the lower limb of patients in a septic state, we did not carry out amputation of the lower limb. Both patients finally died of hepatic coma and septic shock due to necrosis of the small intestine.

DISCUSSION

In this report, we demonstrated the superior early and long-term results of PB-MNCs therapy for critical limb ischemia. Thanks to PB-MNCs therapy, rest pain was diminished or decreased in 91% of the patients and ischemic ulcer formation was cured without recurrence in 60% of the legs. The actuarial survival rate and freedom from major amputation of the lower limb at 36 months after PB-MNCs therapy were 73% and 92%, respectively.

According to the ACC/AHA guidelines,¹⁾ the prognosis of critical limb ischemia is relatively poor. Twenty-five percents of the patients require major amputation of the diseased limb, and only 50% of the patients will be alive with two limbs at one year after diagnosis of critical limb ischemia. It is, therefore, important to develop new treatment for CLI, especially those who are not indicated for surgery. Recently, angiogenetic therapeutic methods using bone marrow mononuclear cells (BM-MNCs) for CLI have been shown to have beneficial effects.^{6, 7)} However, one-third of the treated patients did not respond

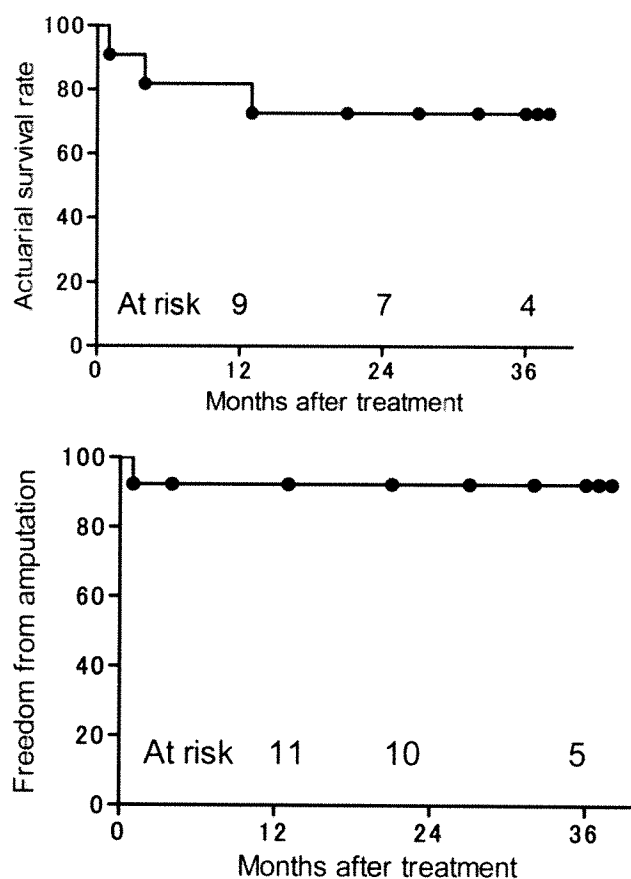


Fig. 3 Actuarial survival rate (A) and freedom from major amputation of the lower limb (B) at 36 months after PB-MNCs therapy were 73% and 92%.

well, and it is sometimes difficult to use BM-MNCs in the high-risk patients because general anesthesia is required to obtain a significant number of BM-MNCs. Therefore, less-invasive PB-MNCs therapy has been developed to treat CLI.

Hoshino et al.²⁾ described the efficacy of PB-MNCs therapy for CLI patients with diabetes mellitus on hemodialysis. Skin perfusion pressure, skin temperature, and ABI were maintained at a higher level than those at baseline during the 6 months after PB-MNCs therapy. Huang et al.³⁾ compared the efficacy between BM-MNCs therapy and PB-MNCs therapy to treat CLI. According to their study, comparative analysis revealed that at 12 weeks after cell implantation therapy, improvement of ABI, skin temperature, and rest pain was significantly better in PB-MNCs patients than BM-MNCs patients. Although the exact explanation was not clear, the authors speculated that the role of G-CSF used in PB-MNCs therapy might have exerted some favorable effects to

promote superior results, because G-CSF induced the production of several growth factors. Although other reports⁸⁻¹⁰⁾ have also described the beneficial effects of PB-MNCs therapy, only a few reports have so far examined the long term effects of PB-MNCs therapy. Horie et al.⁵⁾ reported a 2 year survival rate of 65% and a 1 year amputation free rate of 70% in ASO patients after PB-MNCs therapy.

We followed 11 patients for over 3 years and observed 3 deaths and one major amputation after PB-MNCs therapy. Two patients among the 3 dead patients underwent hemodialysis for end-stage renal failure. Although one patient died of sepsis at 4 months after treatment, and the other died of a hepatic coma at 12 months after the treatment. One patient underwent major amputation, 2 months after the PB-MNCs therapy, and later died of severe pneumonia. This was the only patient who required major amputation after PB-MNCs therapy, and the remaining 10 patients have not undergone any major amputation, indicating a superior amputation free ratio of 92% at three years after PB-MNCs therapy. We also showed that the time required to enhance the arteries by angiography at the level of the foot-joint was significantly shortened at 1 month after PB-MNCs therapy. Although it is difficult to clarify the exact mechanism responsible for these superior long term effects, once improved micro-circulation induced by PB-MNCs therapy might continue to enhance the favorable effects for local circulation of the ischemic limbs.

Our study has, therefore, demonstrated that G-CSF-induced PB-MNCs therapy showed striking early and long term results, however, because of the relatively small number of patients enrolled this study, more patients and a longer follow-up duration will be required to confirm our data.

REFERENCES

- 1) Hirsch AT, Haskal ZJ, Hertzler NR, et al. ACC/AHA 2005 Practice Guidelines for the management of patients with peripheral arterial disease (lower extremity, renal, mesenteric, and abdominal aortic): a collaborative report from the American Association for Vascular Surgery/Society for Vascular Surgery, Society for Cardiovascular Angiography and Interventions, Society for Vascular Medicine and Biology, Society of Interventional Radiology, and the ACC/AHA Task Force on Practice Guidelines (Writing Committee to Develop Guidelines for the Management of Patients With Peripheral Arterial Disease); endorsed by the American Association of Cardiovascular and Pulmonary

- Rehabilitation; National Heart, Lung, and Blood Institute; Society for Vascular Nursing; TransAtlantic Inter-Society Consensus; and Vascular Disease Foundation. *Circulation* 2006; **113**: e463-654 Review.
- 2) Hoshino J, Ubara Y, Hara S, et al. Quality of life improvement and long-term effects of peripheral blood mononuclear cell transplantation for severe arteriosclerosis obliterans in diabetic patients on dialysis. *Circ J* 2007; **71**: 1193-8.
- 3) Huang PP, Yang XF, Li SZ, et al. Randomised comparison of G-CSF-mobilized peripheral blood mononuclear cells versus bone marrow-mononuclear cells for the treatment of patients with lower limb arteriosclerosis obliterans. *Thromb Haemost* 2007; **98**: 1335-42.
- 4) Kajiguchi M, Kondo T, Izawa H, et al. Safety and efficacy of autologous progenitor cell transplantation for therapeutic angiogenesis in patients with critical limb ischemia. *Circ J* 2007; **71**: 196-201.
- 5) Horie T, Onodera R, Akamatsu M, et al. Long-term clinical outcomes for patients with lower limb ischemia implanted with G-CSF-mobilized autologous peripheral blood mononuclear cells. *Atherosclerosis* 2010; **208**: 461-6 Epub 2009 Aug 3.
- 6) Tateishi-Yuyama E, Matsubara H, Murohara T, et al. Therapeutic angiogenesis for patients with limb ischaemia by autologous transplantation of bone-marrow cells: a pilot study and a randomised controlled trial. *Lancet* 2002; **360**: 427-35.
- 7) Yamamoto K, Kondo T, Suzuki S, et al. Molecular evaluation of endothelial progenitor cells in patients with ischemic limbs: therapeutic effect by stem cell transplantation. *Arterioscler Thromb Vasc Biol* 2004; **24**: e192-6 Epub 2004 Oct 14.
- 8) Huang P, Li S, Han M, et al. Autologous transplantation of granulocyte colony-stimulating factor-mobilized peripheral blood mononuclear cells improves critical limb ischemia in diabetes. *Diabetes Care* 2005; **28**: 2155-60.
- 9) Ishida A, Ohya Y, Sakuda H, et al. Autologous peripheral blood mononuclear cell implantation for patients with peripheral arterial disease improves limb ischemia. *Circ J* 2005; **69**: 1260-5.
- 10) Zhou B, Bi YY, Han ZB, et al. G-CSF-mobilized peripheral blood mononuclear cells from diabetic patients augment neovascularization in ischemic limbs but with impaired capability. *J Thromb Haemost* 2006; **4**: 993-1002.

» Case Report «

A Case of a Mycotic Aneurysm of the Superficial Femoral Artery Infected by Mixed Bacterial Species

Thushan Dhananja Gooneratne, Suhashini Sriskantha, and Mandika Wijeyaratne

A 65-year-old woman, recently diagnosed with diabetes, presented with fever and a warm, pulsatile, tender mass over the medial aspect of her left thigh. She gave a history of diarrhea two weeks earlier. All lower limb pulses were present. CRP was 18.3 mg/l with evidence of neutrophil leukocytosis.

Contrast angiography demonstrated a saccular aneurysm in her left superficial femoral artery (SFA). The aneurysm and surrounding infected, necrotic muscle was excised, and the limb was re-vascularized in-situ. Cultures from the aneurysmal wall grew both coliform bacilli and staphylococcus aureus. A mycotic aneurysm of the SFA, following a previous gastroenteritis, harbouring both staphylococcal and coliforms, makes this case unique.

Keywords: mycotic, aneurysm, rare

INTRODUCTION

A mycotic aneurysm is a localized, irreversible arterial dilatation due to destruction of the vessel wall by infection. It is a serious, clinical condition with significant morbidity and mortality, first described by Osler in 1885.¹⁾

Mycotic aneurysms can arise after an infection of a previously healthy artery wall, or through secondary infection of a pre-existing aneurysm. Historically, mycotic aneurysms have been documented in most sites, including the abdominal aorta, femoral artery, as well as superior mesenteric, brachial, iliac, and carotid arteries.²⁾ Mycotic aneurysms of the femoral artery, however, are a rarity, accounting for merely 0.8% of all aneurysms.²⁾

Gram positive organisms, such as *Staphylococcus* and *Streptococcus* species, as well as gram negative *Salmonella*, are some of the commonly cultured pathogens. A mycotic aneurysm of the superficial femoral artery (SFA), following a previous gastroenteritis and harbouring both

staphylococcal and coliforms, makes this case even rarer and all the more unique.

CASE DESCRIPTION

A 65-year-old woman, recently diagnosed with diabetes, presented with fever and a warm, pulsatile, tender mass over the medial aspect of her left thigh with overlying bluish discoloration. There was no preceding history of trauma, superficial infection or any medication that would predispose her to infections. However, she had had right lower quadrant abdominal pain and fever two weeks earlier. There was no associated blood or mucous passage.

On examination, she was febrile and had a pulsatile, tender, rapidly enlarging mass over the medial aspect of her left thigh with bluish discoloration of the overlying skin. All her lower limb pulses were present. Preliminary investigations revealed a CRP value of 18.3 mg/l with a white blood cell count of 22700 / μ l with neutrophil leukocytosis. Her fasting blood glucose level was 6.8 mmol/l and within normal parameters.

Contrast angiography, preceded by color duplex, localized a saccular aneurysm in the SFA, 6 cm from its origin (**Figs. 1 and 2**). Surgical exploration was undertaken, considering the rapid expansion and septic nature of the lesion. The entire aneurysm with a segment of SFA and its surrounding infected, necrotic muscle was excised.

University Surgical Unit, Faculty of Medicine, Colombo, Sri Lanka

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Corresponding author: Thushan Dhananja Gooneratne. 13/1, Sri Saranankara Road, Kalubowilla, Dehiwala, Sri Lanka
Tel: +94772004092
E-mail: thushey@hotmail.com



Fig. 1 Contrast angiography localizing the aneurysm in the left superficial femoral artery to 6 cm from its origin.



Fig. 2 Digitally subtracted image demonstrating the saccular nature of the aneurysm.

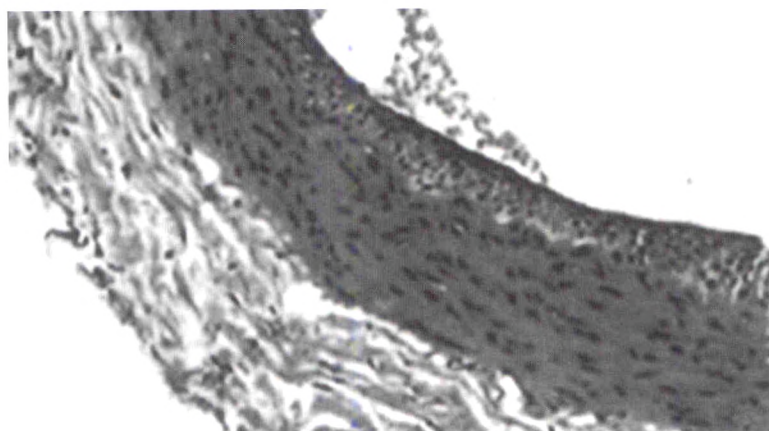


Fig. 3 Histopathology revealing arterial wall musculature infiltrated by neutrophils, with areas of calcification and mucinous degeneration.

The limb was re-vascularized using a proximal to distal SFA reverse saphenous vein graft, which was inserted through uninfected tissue.

Histopathology revealed arterial wall musculature infiltrated by neutrophils, with areas of calcification and mucinous degeneration (**Fig. 3**). The surrounding skeletal muscles, too, showed necrosis and diffuse infiltration with neutrophils and abscess formation. Culture taken

from the aneurysmal wall grew both coliform bacilli and staphylococcus aureus. Serum agglutination test for salmonella serotypes was negative.

The postoperative period was uneventful. The CRP fell to 8.7 mg/dL, and the WBC fell to 13700, 1 week after the aneurysmal operation. At the time of discharge, the values had further declined to normal parameters. Patient is to be followed up at the surgical clinic as an outpatient.

DISCUSSION

We report a case of a mycotic aneurysm of the SFA as a delayed complication of gastroenteritis due to coliform bacilli. Although she had a rapid recovery from the diarrheal episode, bacteremia from gastroenteritis probably ensued and established a vascular focus for infection.

The commonest organisms involved are *Staphylococcus* (30%) followed by *Salmonella* (10%),³⁾ whereas, *Escherichia coli* is the commonest cause of bacteraemia induced mycotic aneurysms.³⁾ This patient demonstrates an example of a microbiological growth, cultured from the aneurysmal wall consisting of both *staphylococcus* and coliform species.

The reason as to why she harbored a mixed growth can be explained by the immuno-compromised state of the patient owing to diabetes mellitus. The primary focus of sepsis remains to be the gastroenteritis, which was incompletely managed. A second infection through the cannula site may account for the staphylococcal septicemia. Interestingly, the patient revealed very little symptoms of harboring a virulent organism like *Staphylococcus aureus*.

Her presentation was typical of that of a mycotic aneurysm, with a pulsatile mass (52%), bruit (50%) and fever (48%). The diagnosis was also supported by leukocytosis (64%–71%).⁴⁾

Surgical options for operative treatment of mycotic aneurysm include either extra-anatomic or in-situ reconstruction.⁵⁾ There is, however, no clear indication for a certain operative technique, and the decision is usually made according to the surgeon's preference.⁶⁾

Extra-anatomic reconstruction requires multiple operations to restore the natural direction of blood flow, whereas in-situ reconstruction offers a definitive solution via a single operation.⁷⁾ However, in-situ reconstruction has been discouraged due to concerns regarding anastomotic or graft destruction by persistent infection.⁸⁾ In recent years, in-situ reconstruction has slowly gained popularity.⁷⁾ Currently, endovascular repair has emerged as an alternative therapy for patients who have high operative risks that prohibit open surgery.⁹⁾

Taking into consideration, the general health status of the patient, the site of arterial infection and local surrounding, we too opted for an in-situ reconstruction. All infected and devitalized tissue was excised at the time of surgery. We were able to ensure successful graft patency by preserving a 3 cm long, macroscopically healthy arterial segment both proximal and distal to the

aneurysm. Even though the anastomosis had taken place in its wound bed, containing infected arterial and muscle tissue, the patient recovered well and was discharged for future follow up.

CONCLUSION

A pulsatile vascular mass with evidence of inflammation and infection is most often a mycotic aneurysm, even if in an uncommon site.

This patient demonstrated a mixed microbiological growth of both *staphylococcus* and coliform species and maybe explained by her immune-compromised state owing to diabetes mellitus. The primary focus of sepsis appears to be the gastroenteritis, which was incompletely managed. A second infection through a cannula site may account for the staphylococcal septicemia.

An extra-anatomic reconstruction is not essential for mycotic aneurysms. Case experience recommends adequate debridement with preservation of a 3-cm long, macroscopically healthy arterial margin for future in-situ reconstructions of mycotic aneurysms.

REFERENCES

- 1) Osler W. The Gulsontonian lectures on malignant endocarditis. *Brit Med J* 1885; 1: 467-70.
- 2) Jewkes AJ, Black J. Infection of an abdominal aortic aneurysm from an appendix abscess. *J Cardiovasc Surg (Torino)* 1989; 30: 870-2.
- 3) Schrander VD, Meer AM, Guit GL, et al. Mycotic aneurysm of the suprarenal abdominal aorta. *Neth J Med* 1994; 44: 23-5.
- 4) Wilson RS, Bennett KR. Mycotic femoral aneurysm. *J Miss State Med Assoc* 2007; 48: 131-2.
- 5) Lin CY, Hong GJ, Lee KC, et al. Successful treatment of *Salmonella* mycotic aneurysm of the descending thoracic aorta. *Eur J Cardiothorac Surg* 2003; 24: 320-2.
- 6) Gomes MN, Choyke PL, Wallace RB. Infected aortic aneurysms. A changing entity. *Ann Surg* 1992; 215: 435-42.
- 7) Pasic M, Carrel T, von Segesser L, et al. In situ repair of mycotic aneurysm of the ascending aorta. *J Thorac Cardiovasc Surg* 1993; 105: 321-6.
- 8) Forbes TL, Harding GE. Endovascular repair of *Salmonella* infected abdominal aortic aneurysms: a word of caution. *J Vasc Surg* 2006; 44: 198-200.
- 9) Sayed S, Choke E, Helme S, et al. Endovascular stent graft repair of mycotic aneurysms of the thoracic aorta. *J Cardiovasc Surg (Torino)* 2005; 46: 155-61.

» Case Report «

A Case of LMT Reconstruction Using Superficial Femoral Artery Graft in the Patient with Type A Acute Aortic Dissection

Shota Yasuda, MD, Kiyotaka Imoto, MD, PhD, Keiji Uchida, MD, PhD, Daisuke Machida, MD, and Hiromasa Yanagi, MD, PhD

A 76-year-old woman underwent a Bentall procedure for acute aortic dissection. A dissection involving half of the proximal portion of the left main coronary artery trunk was confirmed. The dissected site was resected, and a section of the superficial femoral artery was harvested and used as an interposition graft between conduit and the residual left main trunk. Two years after surgery, the graft remained well patent. If the coronary dissection involves only the left main artery trunk, the superficial femoral artery should be used as an artery graft for the anatomical reconstruction, potentially leading to better early and late outcomes.

Keywords: coronary artery dissection, superficial femoral artery graft, bentall's operation

INTRODUCTION

Aortic root replacement is indicated in patients with acute aortic dissection who have annuloaortic ectasia or external rupture of the aortic root. The coronary ostium is generally reconstructed by the button technique, but reconstruction is challenging if the dissection involves a coronary artery. We describe our experience with a patient in whom external rupture of the left main trunk was found during surgery for aortic dissection. The affected site was removed and reconstructed with a superficial femoral artery graft, resulting in a good outcome.

CASE REPORT

The patient was a 76 year-old woman with a history of hypertension and asthma (being treated with oral

therapy). Her family history was not relevant to the current disorder. The patient presented to a local physician because of chest pain and was admitted for follow-up observation. Subsequently, the chest pain resolved, but contrast-enhanced computed tomography (CT) of the chest revealed a dissection of the ascending aorta, with an increase in lumen diameter. Retention of pericardial fluid was noted. The patient was referred to our center to undergo surgery. On admission, the height was 146 cm, the body weight was 43 kg, the blood pressure was 157/97 mmHg, and the pulse rate was 120 beats per minute. The patient did not have chest pain at presentation. On chest auscultation, there was no cardiac murmur.

Chest radiography showed that the cardiothoracic ratio was 63.5%, indicating an upper mediastinal extension. On 12-lead electrocardiography, the sinus rhythm was normal. The heart rate was 120 beats per minute. The axis of the heart was normal, with no ST-segment deviation. Contrast-enhanced CT of the chest revealed a thrombosed-type acute aortic dissection. An ulcer-like projection was found in the descending aorta. The dissection was classified as DeBakey type IIIR (**Fig. 1**). The diameter of the ascending aorta had increased to 55 mm, with pericardial fluid retention. The pericardial fluid appeared to be bloody because the CT attenuation

Cardiovascular Center, Yokohama City University Medical Center, Yokohama, Kanagawa, Japan

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Corresponding author: Shota Yasuda, MD. Cardiovascular Center, Yokohama City University Medical Center, 4-57, Urafunecho, Minami-ku, Yokohama 232-0024, Japan
Tel: +81-45-261-5656, Fax: +81-45-261-9162
E-mail: shorty@mtj.biglobe.ne.jp

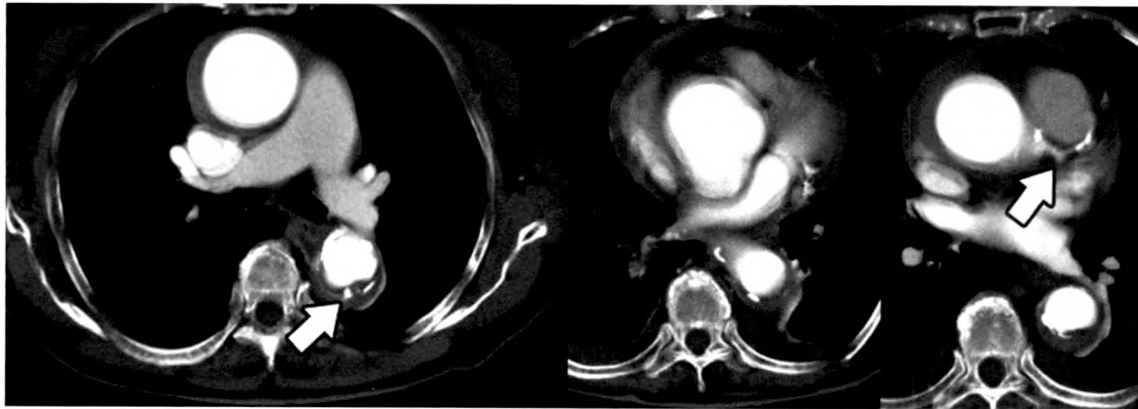


Fig. 1

A: A dissection involving half of the proximal portion of the left main coronary artery trunk was confirmed at surgery. The diameter of the ascending aorta had increased to 55 mm. An ulcer-like projection was found in the descending aorta (white arrow).
B: Pericardial fluid retention was evident. The CT attenuation value of the pericardial fluid ranged from 40 to 50 Hounsfield units, suggesting rupture of the aorta.
C: A cross-sectional slice of the LMT (white arrow). Dissection of the LMT was unclear.
 LMT: left main trunk; CT, computed tomography

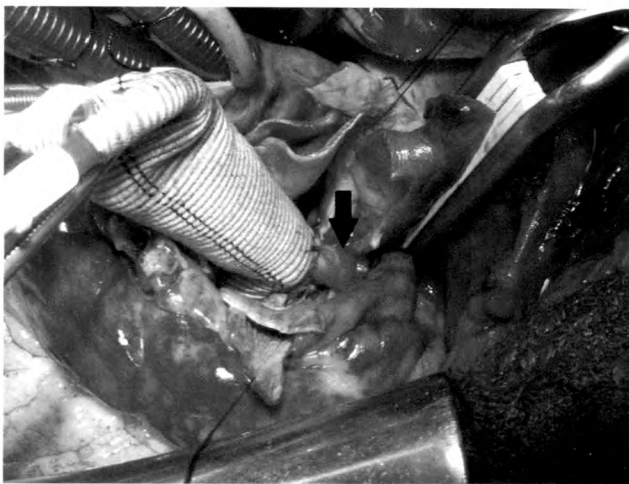


Fig. 2 Intraoperative findings.
 The superficial femoral artery graft was anastomosed end-to-end to the conduit.
 (Black arrow: superficial femoral artery graft)

value of the pericardial fluid ranged from 40 to 50 Hounsfield units, suggesting a rupture of the ascending aorta. An emergency operation was thus performed.

Transesophageal ultrasonography showed that the diameter of the sinus of Valsalva had increased to 58 mm. We therefore decided to perform an aortic root replacement. Artificial grafts were anastomosed end-to-side to the right axillary artery. The pericardium was incised after extracorporeal circulation had begun. The pericardial fluid was bloody, but there was no evidence of

active bleeding. The ascending aorta was clamped. When a coronary artery cuff was formed, the dissection was found to involve about half of the circumference of the left main trunk. A rupture hole was noted in the adventitia around the left main trunk (LMT). Because there were no other adventitial ruptures, this site was considered the source of bleeding.

Conventional reconstruction using the button technique was not feasible. On further examination, the dissection was found to involve only the proximal half of the entire length of the left main trunk. We decided to resect the involved portion. Because it was considered difficult to directly anastomose the left coronary artery to a conduit, we used a portion of the left superficial femoral artery as an interposition graft. About 4 cm of the left superficial femoral artery was harvested. The left superficial femoral artery was reconstructed using a left great saphenous vein. Because the diameter of the aortic annulus was 23 mm, a 19-mm St. Jude Medical Mechanical Hemodynamic Plus[®] prosthesis was placed in a 22-mm Hemashield[®] straight graft to form a conduit. The conduit was sutured to the aortic valve annulus with 13 2-0 Ethibond EXCEL[®] sutures. The superficial femoral artery graft was anastomosed end-to-end to the distal portion of the left main trunk, using 6-0 Prolene[®] sutures. Next, the proximal end of the superficial femoral artery graft was anastomosed end-to-side to the conduit, using 5-0 Prolene[®] sutures (**Fig. 2**). The length of the interposition graft was about 2 cm. Subsequently, low-temperature

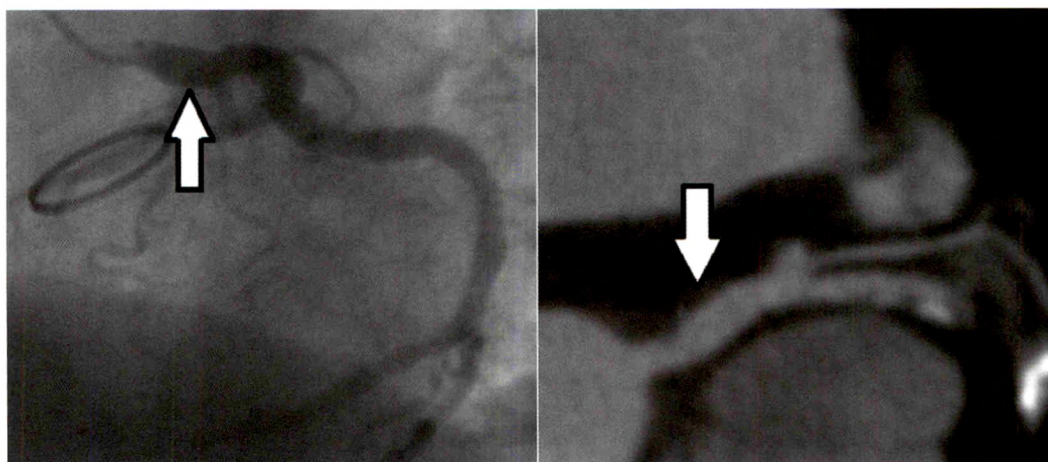


Fig. 3

A: Postoperative coronary angiography showed no anastomotic strictures.
B: Computed tomography of the coronary artery about 2 years after the operation revealed good patency of the superficial femoral artery graft.
 (White arrow: superficial femoral artery graft)

circulatory arrest was performed, and the distal end of the ascending aorta was reinforced with a Teflon felt strip and anastomosed to the conduit. The duration of aortic clamping was 312 minutes.

After the completion of aortic root replacement, the patient was easily weaned from extracorporeal circulation. The durations of extracorporeal circulation (377 minutes) and surgery (625 minutes) were prolonged, leading to severe cardiac edema. Primary sternal closure was, therefore, difficult, and the patient was transferred to the intensive care unit without closing the sternum. On the third postoperative day, secondary sternal closure was performed.

Coronary angiography before discharge showed no anastomotic stricture (**Fig. 3**). About 2 years after surgery, coronary artery CT showed no clinically significant strictures (**Fig. 3**). The patient is now being followed up on an outpatient basis.

DISCUSSION

Our patient required aortic root replacement because of type A acute aortic dissection with an enlarged sinus of Valsalva. Reconstruction by the Bentall technique was precluded by adventitial rupture of the LMT. We initially considered ligation of the left main trunk, followed by bypass surgery with a great saphenous vein graft. However, we decided to resect the dissected left main trunk and then perform anatomical reconstruction using the autologous superficial femoral artery as an interposition graft.

Three alternative methods can be used for coronary artery reconstruction: graft interposition, coronary cuff reinforcement, and CABG. Piehler et al. performed coronary artery reconstruction using small-caliber artificial grafts,¹⁾ but anastomosis to the artificial graft was difficult because the distal diameter of the left main trunk was less than 5 mm. A technique using the great saphenous vein as an interposition graft has been proposed, but carries the risk of kinking if the graft is too long.²⁾ The development of late graft disease can be life-threatening. LMT cuff reinforcement is a commonly used technique. In patients with adventitial rupture of the LMT, however, the use of a Carrel patch is not feasible. Ligation and bypass with a saphenous vein graft is simple and straightforward. However, this technique carries the risk of graft disease because artificial vessel grafts are used as the reconstructed aorta.

The superficial femoral artery can be easily harvested, has an adequate wall thickness, and is easy to handle even in deep regions; anastomosis is thus relatively easy to perform. The caliber of an autologous superficial femoral artery graft is only slightly larger than that of the distal end of the left main trunk, and the use of an autologous graft decreases the risk of graft disease.

To our knowledge, a reconstruction procedure similar to the one described in this study has not been documented previously. Morimoto et al. reported that interposition methods are useful,³⁾ and our techniques may be advantageous in patients who undergo root replacement in second cardiac operation. However, the superficial

femoral artery has a relatively higher risk of atherosclerosis, potentially leading to stenosis or occlusion.⁴⁾ Two years after surgery, graft patency is good in our patient, but close follow-up is required to ensure that the graft remains patent.

CONCLUSIONS

In our patient, dissection involving the main trunk of the left coronary artery was detected during surgery for aortic dissection. The dissection was resected, and reconstruction was done with a superficial femoral artery graft. The superficial femoral artery was used for the reconstruction because it is anatomical and associated with long-term patency. Outcomes are good, 2 years after surgery.

REFERENCES

- 1) Piehler J, Pluth J. Replacement of the ascending aorta and aortic valve with a composite graft in patients with nondisplaced coronary ostia. *Ann Thorac Surg* 1981; **33**: 406-9.
- 2) Neri E, Toscano T, Papalia U, et al. Proximal aortic dissection with coronary malperfusion: presentation, management, and outcome. *J Thorac Cardiovasc Surg* 2001; **121**: 552-60.
- 3) Morimoto H, Aomi S, Saito S, et al. Redo aortic root surgery: Clinical validation of prosthetic valve preservation and coronary graft interposition technique. *J Tokyo Wom Med Univ* 2008; **78**: 513-8.
- 4) Walden R, Adar R, Rubinstein ZJ, et al. Distribution and symmetry of arteriosclerotic lesions of the lower extremities: an arteriographic study of 200 limbs. *Cardiovasc Intervent Radiol* 1985; **8**: 180-2.

» Case Report «

The Management of Persistent Sciatic Artery Aneurysm with Lower Extremity Ischemia: A Case Report

Bin Chen, MD, Zhenyu Shi, MD, Yuqi Wang, MD, Weiguo Fu, MD, and Weimiao Li

We report a case of lower extremity ischemia caused by a persistent sciatic artery aneurysm. The patient was successfully treated with a ringed expanded polytetrafluoroethylene (ePTFE) graft and recovered uneventfully. The graft was patent during the follow-up and no signs of kinking or restenosis.

Keywords: persistent sciatic artery, aneurysm, duplex scanning

INTRODUCTION

Persistent sciatic artery (PSA) is a rare congenital vascular anomaly with an incidence of 0.03%–0.06%.¹⁾ The anatomic characteristic of the artery has brought various complications such as atherosclerosis and aneurysm formation.²⁾ The latter had a relatively high incidence of 48% and could be associated with lower extremity ischemia which may result in amputation.¹⁾ We report a PSA aneurysm with lower extremity ischemia treated with a ringed graft.

CASE HISTORY

A 62-year-old underweight woman complained of a pulsatile mass in the right buttock and claudication for 9 months without any related recent trauma or surgery. The ankle brachial index was 0.77, indicating mild ischemia. She experienced coldness and paresthesia of the right leg. Examination of her right lower extremity revealed a weak palpable femoral artery pulse but no distal pulses. The pulsatile mass in the buttock was about 5 cm with a mild tender and clear boundary. The contralateral arteries were all clearly palpable.

Department of Vascular Surgery, Zhongshan Hospital, Fudan University, Shanghai, China

Received: April 27, 2011; Accepted: July 21, 2011
Corresponding author: Weimiao Li. Department of Vascular Surgery, Zhongshan Hospital, Fudan University, 180 Fenglin Road, Shanghai 200032, China
Tel: +86-21-6404-1990, Fax: +86-21-6403-7183
E-mail: neuronchip@163.com

Duplex ultrasound (DU) scanning and computed tomography angiography (CTA) were conducted. DU scanning showed a semi-thrombotic enlargement of the sciatic artery with both proximal and distal arterial wall hypertrophied. The aneurysm sac was shuttle-shaped and 4 cm in diameter. Subsequent CTA revealed the panorama of the PSA aneurysm (**Fig. 1**). As illustrated by the images, the aneurysmal artery has a stenosis at the distal neck (**Fig. 1**, arrow) which may be responsible for the lower extremity ischemia. The PSA had substituted the femoral artery as the main blood supply of the lower extremity. The popliteal artery was the continuation of the PSA. Compared to the contralateral normal femoral artery system, the affected arteries were circuitous and hypoplasia, which may aggravate the distal ischemia.

Open surgery was performed with a ringed graft (Gore-Tex, USA) in a prone position. An incision was made in the right buttock over the course of the PSA. The aneurysm sac was exposed entirely with two ends dissected till normal segments. The aneurysmal sac was then opened and transplantation was performed using an 8-mm graft within the sac. The graft ends were both sutured to the normal arterial segments, and the wall of the sac was closed over the graft (**Fig. 2**). The whole procedure was conducted within the aneurysm sac to minimize the adverse impact on surrounding tissues, such as the sciatic nerve. Six days later, the ankle brachial index was 0.82, and previous clinical ischemic symptoms had improved subjectively.

Pre-discharge DU scanning was carried out and showed a patent graft with a triphasic flow pulse (**Fig. 3A**). The patient made an uncomplicated recovery with

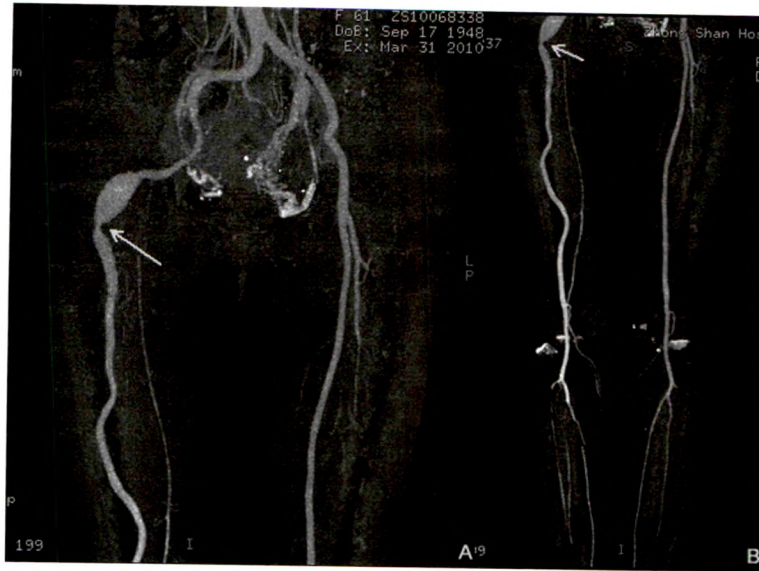


Fig. 1 Computed tomography angiography of the PSA aneurysm. (A) The aneurysmal PSA and stenosis at the distal neck. (B) The anatomy of lower extremity arterial system.
PSA: persistent sciatic artery

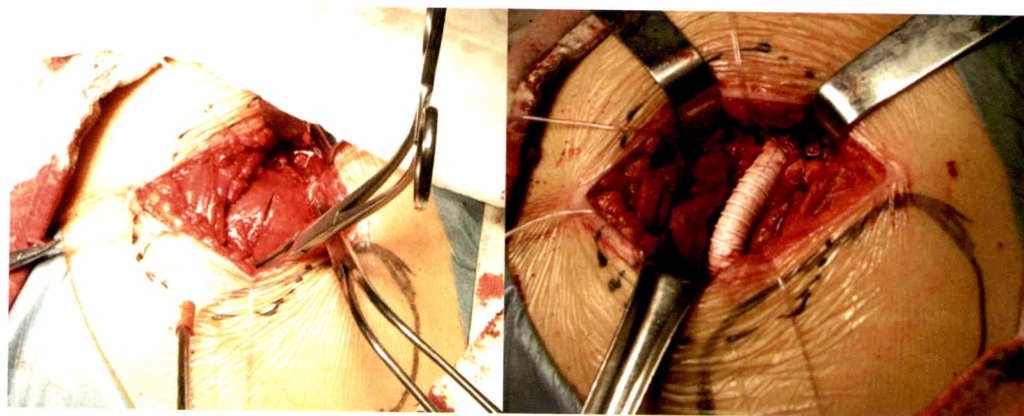


Fig. 2 The transplantation of ringed graft within the PSA aneurysm sac.
PSA: persistent sciatic artery

improvement of ischemia symptoms. Three months later, the patient came back without any related complaints, and DU scanning suggested no kinking or restenosis (**Fig. 3B**). One year later, she reported no recurrent symptoms via telephone.

DISCUSSION

During early embryonic development, the sciatic artery is the axial artery of the lower limb which supplies the entire leg. When the femoral artery system develops and become dominant, the sciatic artery involutes. But if normal development fails, the sciatic artery may persist,

instead of regressing supplying the lower extremity. The anomaly is rare with the incidence of 0.03%–0.06%, but related complications may result in amputation in 8% of the cases.¹⁾ The PSA originates from the internal iliac artery and runs through the sciatic notch entering the adductor magnus along the dorsal aspect of the lower extremity. There are two types of PSA recognized: complete sciatic artery is the continuation of the internal iliac artery and turn into popliteal artery in the popliteal fossa; an incomplete type is just like the sciatic artery remnants acting as the collateral branches connecting the internal iliac artery and popliteal artery while a complete femoral artery system is the dominant blood supplier.

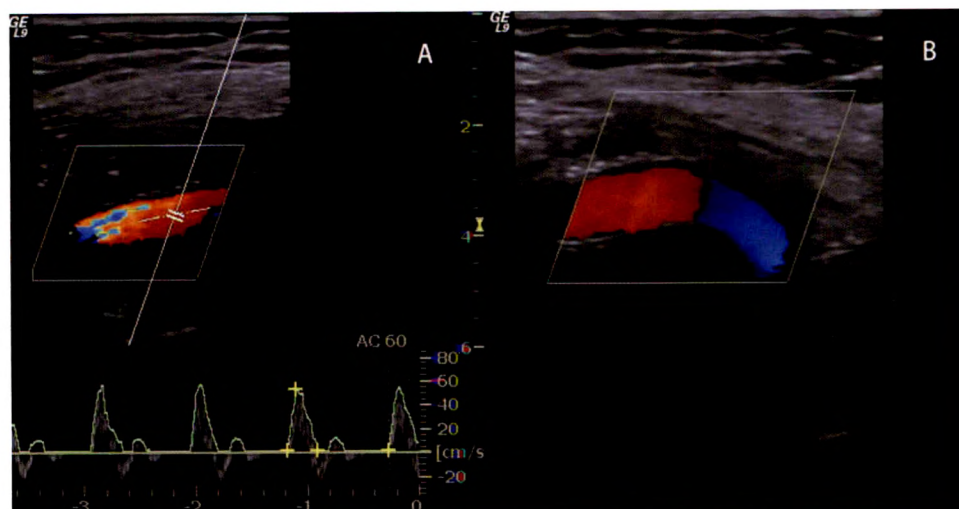


Fig. 3 (A) Pre-discharge DU scanning showed a patent graft with triphasic pulse. (B) The distal anastomosis at 3 months after graft interposition, DU showed a patent in-graft flow. DU: duplex ultrasound

The PSA is susceptible to aneurysm formation which is probably due to the superficial position in the buttock and repeated external trauma.²⁾ A PSA aneurysm may result in severe complications, including neurologic symptoms due to sciatic nerve compression, tenderness in the buttock, ipsilateral lower extremity ischemia and rupture.³⁾

The treatment for PSA aneurysm depends on the anatomy and symptoms presented. Options for intervention include graft interposition, extra-anatomic bypass, embolization and endovascular stent implantation. Open surgery for PSA remains controversial and is not recommended for asymptomatic patients.^{1, 4, 5)} The drawback is mostly because of the close proximity of the PSA to the sciatic nerve, which may contribute to iatrogenic adverse outcomes.

Here, we present a patient who had a complete PSA with a hypoplasia femoral artery system. Therefore, the PSA should be preserved or aneurysm be excluded for extremity blood supply. Coil embolization won't be appropriate method for this case. The advantages of graft interposition and endovascular stent implantation are less invasive operation and shorter procedure time compared to bypass surgery. Considering the position of the aneurysm and the slim somatotype, we assume the endovascular stent may be fractured or distorted and thrombosed. As the long-term results were not as sure as the open surgery, we at last chose the graft transplantation. A ringed ePTFE graft was appointed for the external support to increase the graft resistance to compression and reduce kinking risk. In addition, the circuitous part

of the artery was replaced by the graft and guarantees the blood flow. The whole procedure was completed within the aneurysm sac to maintain the sciatic nerve intact and the patient recovered without any neurologic symptoms.

As endovascular therapy is widely used for PSA management,^{1, 6, 7)} open surgery still has its own merits and should be taken into consideration in some special cases.

REFERENCE

- 1) van Hooft IM, Zeebregts CJ, van Sterkenburg SM, et al. The persistent sciatic artery. *Eur J Vasc Endovasc Surg* 2009; **37**: 585-91 Epub 2009 Feb 20.
- 2) McLellan GL, Moretti LB. Persistent sciatic artery: clinical, surgical, and angiographic aspects. *Arch Surg* 1982; **117**: 817-22.
- 3) Ishida K, Imamaki M, Ishida A, et al. A ruptured aneurysm in persistent sciatic artery: a case report. *J Vasc Surg* 2005; **42**: 556-8.
- 4) Steele G Jr, Sanders RJ, Riley J, et al. Pulsatile buttock masses: gluteal and persistent sciatic artery aneurysms. *Surgery* 1977; **82**: 201-4.
- 5) Brantley SK, Rigdon EE, Raju S. Persistent sciatic artery: embryology pathology and treatment. *J Vasc Surg* 1993; **18**: 242-8.
- 6) Jain S, Munn JS, Simoni EJ, et al. Endograft repair of a persistent sciatic artery aneurysm. *EJVES Extra* 2004; **8**: 5-6.
- 7) Wijeyaratne SM, Wijewardene N. Endovascular stenting of a persistent sciatic artery aneurysm via retrograde popliteal approach: a durable option. *Eur J Vasc Endovasc Surg* 2009; **38**: 91-2 Epub 2009 Apr 22.

➤ Case Report ◀

Repeat Operation for Pseudoaneurysm of Left Ventricular Outflow in a Patient with Concomitant Takayasu's Arteritis and Marfan Syndrome

Satoshi Yamashiro, MD, PhD, Yukio Kuniyoshi, MD, PhD, Katsuya Arakaki, MD, Takaaki Nagano, MD, and Yuya Kise, MD

We describe concomitant Marfan syndrome and Takayasu's arteritis complicating a pseudoaneurysm of the left ventricular outflow that developed after aortic root reconstruction. A patient was admitted with a high fever four months after initial root reconstruction that included valve sparing (reimplantation) as well as coronary artery reconstruction using a Carrel's button technique. Computed tomography revealed a pseudoaneurysm at the posterior side of the aortic root. We applied a modified Bentall procedure including coronary artery reconstruction using the Piehler technique. Pathological assessment of a specimen of the aorta revealed no central medial necrosis, but significant lymphocytic infiltration and thick fibrous adventitia indicating Takayasu's arteritis. This case was unique in terms of having simultaneous Takayasu's arteritis and cardiovascular manifestations of Marfan syndrome that were surgically treated.

Keywords: chronic inflammation, aorta, stenosis, connective tissue disease

Takayasu's arteritis is chronic inflammation of the aorta, its branches, and the pulmonary artery that leads to stenosis/occlusion or dilation. Cardiovascular complications such as aortic valve regurgitation and aneurysmal dilation of the aortic root can be fatal. The most serious complication after root reconstruction for Takayasu's arteritis is dehiscence of the anastomotic site.¹⁻⁴⁾ We describe a patient with Takayasu's arteritis associated with Marfan syndrome who underwent valve sparing root reconstruction for annulo-aortic ectasia with aortic regurgitation, but who required a repeated operation to treat a pseudoaneurysm five months later.

CASE REPORT

A 19 year-old man with annulo-aortic ectasia, accompanied by an aneurysm of the ascending aorta and aortic arch and Marfan syndrome, had undergone root reconstruction and total arch replacement using the elephant trunk method. Preoperative computed tomography (CT) identified aneurysmal dilation from the Sinus of Valsalva to the arch aorta, and stenosis of the left subclavian artery (Fig. 1A). Ultrasound echocardiography revealed mild aortic valve regurgitation. The initial root reconstruction included valve sparing (David II) and coronary artery reconstruction using a Carrel's button technique. He had also undergone total arch replacement using the elephant trunk method with simultaneous reconstruction of the left subclavian artery (Fig. 1B). The postoperative course of this patient was unusual. A high fever persisted despite the absence of an obvious, infectious focus, according to pathological and bacterial analyses. The serum concentration of C-reactive protein (CRP) remained elevated despite negative bacterial cultures. Nineteen days after the initial operation, a pseudoaneurysm that ruptured in the previously cannulated femoral artery was repaired using a

Thoracic and Cardiovascular Surgery Division, Ryukyu University Hospital, Okinawa, Japan

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Correspondence author: Satoshi Yamashiro, MD, PhD. Thoracic and Cardiovascular Surgery Division, Ryukyu University Hospital, 207 Uehara, Nishihara, Okinawa 903-0215, Japan
Tel: +81-98-895-1168; Fax: +81-98-895-1422
E-mail: y3104@med.u-ryukyu.ac.jp



Fig. 1 Preoperative and postoperative computed tomography (CT) images.
A) Preoperative CT image shows aneurysmal dilation from Sinus of Valsalva to arch aorta and stenosis of left subclavian artery (arrow).
B) Postoperative CT image shows good reconstruction of root and arch aorta with simultaneous reconstruction of left subclavian artery (dotted arrow).

graft harvested from the opposite femoral artery because of a suspected infectious pseudoaneurysm. Pathological assessment of a specimen of the right femoral artery included pseudoaneurysm revealed lymphocytic, but not neutrophilic infiltration. Internal medicine physicians suggested the possibility of collagen disease. However, he did not have a high fever, although the elevated CRP persisted even after repairing the pseudoaneurysm of the femoral artery. He was discharged 42 days after the operation despite having persistently high CRP values. Weekly chest computed tomography (CT) during conservative follow up imaging revealed no abnormal findings.

He was re-admitted with a high fever four months after the initial operation. Computed tomography at re-admission revealed a 2-cm pseudoaneurysm at the posterior side of the aortic root (**Fig. 2A** and **2B**), although CT did not recognize this pseudoaneurysm one month previously. The sagittal CT view revealed that the pseudoaneurysm originated from the left ventricular outflow or coronary button of the left coronary artery (**Fig. 2C**). Stenosis was found at the right femoral artery that had been repaired after the initial procedure using an allograft, and a pseudoaneurysm at the right axillary artery that had been cannulated. The preoperative course of this patient was also unusual. Initial laboratory findings at two months before the first operation indicated no inflammatory signs: WBC, 6100/mL; CRP, 0.5 mg/dL. However, a high fever persisted for one week without leu-

kocytosis, but CRP increased to 12.5 mg/dL after cardiac catheterization. We then evaluated the patient for collagen disease. Because antibiotics rapidly abolished the high fever, we investigated its etiology. Negative findings for leukocytosis and bacterial cultures ruled out endocarditis and infectious pseudoaneurysm. Serum procalcitonin was within the normal range. The high CRP level that was found before the initial procedure remained elevated (5–10 mg/dL) and erythrocyte sedimentation rate (ESR) was 105 mm/h. Component C3 and C4 levels were within normal limits and autoantibodies were negative. Therefore, we administered oral corticosteroid (40 mg/day) to control the inflammation. Four days later, the fever subsided, and CRP recovered to within normal limits. We gradually decreased the corticosteroid to 20 mg/day with reference to his CRP and ESR values. We operated on the pseudoaneurysm one month after starting corticosteroid administration. A laceration of about 1 cm transverse that surrounding thickness hard tissue seems to chronic inflammation was located below the left coronary cusp. We applied a modified Bentall procedure, including coronary artery reconstruction using the Piehler technique with a small prosthetic graft, because a severe connective tissue adhesion prevented harvesting of the coronary artery. We constructed an original composite graft with translocation of a mechanical valve to avoid repeated dehiscence of the anastomotic site. The artificial valve was sutured to the vascular prosthesis 1 cm from the edge. The composite

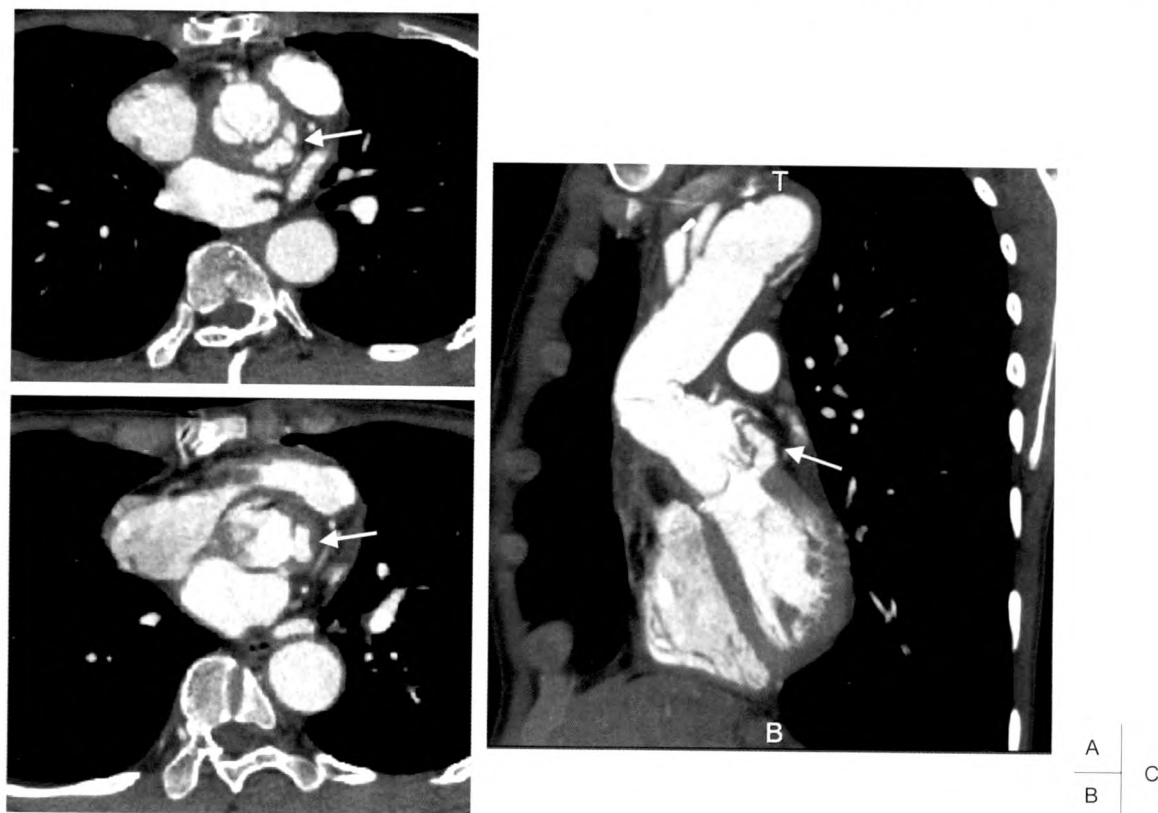


Fig. 2 Computed tomography (CT) images of pseudoaneurysm.
A and B) Images show pseudoaneurysm at posterior side of aortic root (arrow).
C) Sagittal CT view shows that pseudoaneurysm originated from left ventricular outflow.

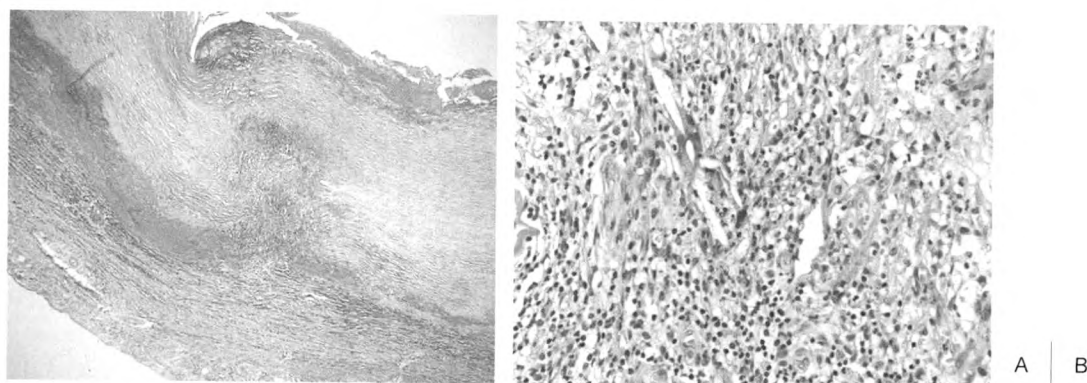


Fig. 3 Pathological findings of specimen.
A and B) Hematoxylin-eosin (HE) staining at $\times 40$ and $\times 100$ magnification, respectively.
 Lymphocytic infiltration is significant.

graft was implanted by suturing the vascular prosthesis with only Teflon felt strip to reinforce around the aortic annulus. Pathological assessment of a specimen of the aorta including annular tissue taken at second procedure revealed significant lymphocytic infiltration and thick, fibrous adventitia but no central media necrosis (**Fig. 3**). The postoperative course was uneventful under

corticosteroid administration. Postoperative CT revealed no abnormalities and he was discharged 21 days after this procedure.

DISCUSSION

Marfan syndrome is an autosomal dominant disorder

of connective tissue involving the skeletal, ocular and cardiovascular systems⁵⁾ that is often complicated by extended aortic aneurysms. Our patient had been diagnosed with Marfan syndrome at another hospital, and this was reconfirmed at the pediatric department of our hospital. His symptoms included typical skeletal signs such as being above average height (180 cm), having dolichostenomelia (elongated limbs), a thin, narrow face and dural ectasia. Moreover, his old twin brother had been diagnosed with Marfan syndrome. Therefore, we considered that he had annulo-aortic ectasia and an arch aneurysm associated with Marfan syndrome. We thus performed root reconstruction including valve sparing (David II) and standard total arch replacement. Preoperative CT identified stenosis of the left subclavian artery, and we, therefore, considered the underlying collagen disease.

Takayasu's arteritis is a nonspecific inflammatory disorder of unknown etiology, involving the aorta, its main branches, and pulmonary arteries, causing arterial stenosis/occlusion or dilation. The aortic root and ascending aorta are dilated in some patients with Takayasu's arteritis.⁶⁾ In our case, causing of aneurysm was not clearly identified to Takayasu's arteritis or Marfan syndrome, but the postoperative arterial events were nevertheless associated with active inflammation due to Takayasu's arteritis. Pathological assessment of a specimen of the aorta taken at the second procedure revealed no central medial necrosis, but significant lymphocytic infiltration and thick, fibrous adventitia indicating Takayasu's arteritis.¹⁾

The most serious complications after AVR or root reconstruction for Takayasu's arteritis are dehiscence of the anastomotic site and the formation of pseudoaneurysms.¹⁻³⁾ Ando et al.⁶⁾ reported a 4.6% (3 of 65 patients) incidence of prosthetic valve detachment after AVR among patients with Takayasu's arteritis. Shiono et al.²⁾ reported that the potential risk for anastomotic dehiscence is much higher in patients with Takayasu's arteritis than in those with dystrophic aneurysms of Marfan syndrome, even during the inactive phase of inflammation. Suzuki et al.⁷⁾ emphasized the importance of reinforcing sutures around the aortic annulus and Carrel's button technique for reconstructing the coronary artery. They also recommended postoperative steroid therapy for active inflammation in patients with Takayasu's arteritis who have undergone several surgical procedures. Some authors also recommend perioperative adjunct steroid therapy to avoid serious anastomotic dehiscence.^{3, 7)} The postoperative course of our patient was unusual. A high fever

persisted despite the absence of an obvious, infectious focus, and serum CRP remained elevated despite negative bacterial cultures. These findings indicated active inflammation in Takayasu's arteritis. Pathological assessment of a specimen of the aorta taken at initial procedure did not reveal specific findings. It might be considered that we operated on the patient in chronic and convalescence period of Takayasu's arteritis and Takayasu's inflammation was activated postoperative period. Controlling the inflammation with corticosteroid immediately after the initial operation might have prevented the postoperative complications. We believe that the pseudoaneurysm was not caused by a technical procedural error because chest CT findings after the first operation were normal, and those at one month before re-admission did not recognize the pseudoaneurysm. The second postoperative course was uneventful when the patient was under corticosteroid administration. We considered that peri-operative steroid therapy for active inflammation in patients with Takayasu's arteritis who have undergone several surgical procedures is important. Matsuura et al.¹⁾ described that active inflammation might be a predictor of pseudoaneurysm. We administered corticosteroid while monitoring the patient's laboratory data (CRP and ESR). He remains on 5 mg/day of oral corticosteroid at 18 months after reoperation.

The translocated Bentall procedure might provide an alternative to composite graft detachment,^{3, 6, 7)} and might be helpful because it allows circumferential fixation outside the aortic wall and double fixation at the aortic annulus, and prosthetic valves do not apply direct pressure to the aortic annulus. Ando et al.⁶⁾ noted that the pressure of valve function directly affects the rigid sewing ring in patients with AVR, which causes a higher detachment rate. We also constructed an original composite graft with translocation of a mechanical valve to avoid repeated dehiscence of the anastomotic site.

This patient was unique in terms of having simultaneous Takayasu's arteritis and cardiovascular manifestations of Marfan syndrome that were surgically treated. To our knowledge, this is a very rare example of concomitant Takayasu's arteritis and Marfan syndrome complicating a pseudoaneurysm after aortic root reconstruction.⁸⁾ Strict follow-up is required to prevent further anastomotic dehiscence.

REFERENCES

- 1) Matsuura K, Ogino H, Kobayashi J, et al. Surgical

- treatment of aortic regurgitation due to Takayasu arteritis: long-term morbidity and mortality. *Circulation* 2005; **112**: 3707-12 Epub 2005 Dec 5.
- 2) Shiono M, Hata M, Sezai A, et al. Reoperation for ascending aortic aneurysm, coronary ostial aneurysm and patent Cabrol trick after bentall operation for aortitis syndrome. *Circ J* 2005; **69**: 861-4.
 - 3) Miyata T, Sato O, Deguchi J, et al. Anastomotic aneurysms after surgical treatment of Takayasu's arteritis: a 40 year experience. *J Vasc Surg* 1998; **27**: 438-45.
 - 4) Pyeritz RE, McKusick VA. The Marfan syndrome: diagnosis and management. *N Engl J Med* 1979; **300**: 772-7.
 - 5) Kalangos A, Baldovinos A, Beghetti M, et al. Ascending aortic aneurysm associated with aortic insufficiency due to Takayasu's arteritis. *Ann Thorac Surg* 1999; **68**: 248-50.
 - 6) Ando M, Kosakai Y, Okita Y, et al. Surgical treatment of Behcet's disease involving aortic regurgitation. *Ann Thorac Surg* 1999; **68**: 2136-40.
 - 7) Stump DC, Califf RM, Topol EJ, et al. Pharmacodynamics of thrombolysis with recombinant tissue-type plasminogen activator. Correlation with characteristics of and clinical outcomes in patients with acute myocardial infarction. The TAMI Study Group. *Circulation* 1989; **80**: 1222-30.
 - 8) Kim KH, Lee C, Ahn H. Successful treatment in a patient with Takayasu's arteritis and Marfan syndrome. *Ann Thorac Surg* 2002; **74**: 908-10.

» Case Report «

A Staged Total Aortic Replacement with Combined Endovascular and Open Surgery: Report of a Case

Manabu Yamasaki, MD, Sunao Watanabe, MD, Kohei Abe, MD, Toshinobu Kazui, MD,
and Kohei Kawazoe, MD

For a 75 year-old man with extensive aortic aneurysm, who had undergone a previous infra-renal abdominal Y-graft, a staged replacement of remaining segments was performed. A hybrid procedure of open-laparotomy debranching of visceral branches and endovascular stentgraft insertion in the thoracoabdominal aorta was performed first, followed by subsequent direct replacement between the proximal ascending and distal arch using cardiopulmonary bypass. Three months thereafter dissection of enlarged proximal descending aorta occurred, for which we performed an emergent endovascular stentgraft deployment which bridged “elephant trunk” of the arch graft and the previous stentgraft. Consequently total aortic replacement was successfully accomplished without any neurological sequela.

Keywords: endovascular surgery, hybrid therapy, dissection

INTRODUCTION

We experience a successful total aortic replacement with staged, combined thoracic endovascular aneurysm repair (TEVAR) and open-surgery strategy for a 75 year-old male patient without adverse neurological events, which we think deserves presentation.

CASE REPORT

A 75 year-old male who had undergone graft replacement using Vascutek Gelweave Y-graft for rupture-impendent infrarenal abdominal aorta four years previously: He showed no characteristic body composition suggestive of Marfan syndrome. Also in the histopathological specimen of the resected aneurysm wall there was no detectable cystic medial necrosis. During postoperative

follow-up, enlargement of the ascending aorta as well as definite aneurysmal dilatation of arch and thoracoabdominal segments (55 mm and 60 mm in diameter, respectively) progressively developed (**Fig. 1**), which necessitated surgical re-intervention. Considering relatively high frequency of postoperative paraplegia/paraparesis in direct open replacement,¹⁾ we chose to perform TEVAR in this area in the first stage, and then to carry out open direct total arch replacement. 1) Under laparotomy, ligation of proximal celiac, superior mesenteric, and both renal arteries were performed (debranching procedure), with concurrent bypass grafting to these vessels with cross-shaped composite vascular graft (Gelsoft 10 mm (Vascutek Terumo Ltd., Inchinnan, Scotland) and Gore-Tex 6 mm graft (W.L.Gore & Associates, Flagstaff, Ariz)) and saphenous vein graft, which was used for the reconstruction of the celiac axis, inflow portion of which was anastomosed into right common iliac segment of previous Y graft (**Fig. 1**). Weeks later, subsequent TEVAR for the aneurysm between the mid-portion of descending thoracic aorta and just above the previous Y-graft, using three stentgrafts (two Gore TAG endografts (W.L.Gore & Associates, Flagstaff, Ariz)(37 mm × 15 cm and TAG 34 mm × 15 cm), and home-made stentgraft (using a noncoated polyester fabric graft(WST graft; Ube, Japan)

Department of Cardiovascular Surgery, Heart Center, St Luke's International Hospital, Tokyo, Japan

Received: July 19, 2011; Accepted: September 12, 2011
Corresponding author: Manabu Yamasaki, MD. Cardiovascular Surgery, St. Luke's International Hospital, 9-1 Akashicho Chuo-ku, Tokyo 104-8560, Japan
Tel: +81-3-5550-7100, Fax: +81-3-5550-7194
E-mail: manayama@luke.or.jp

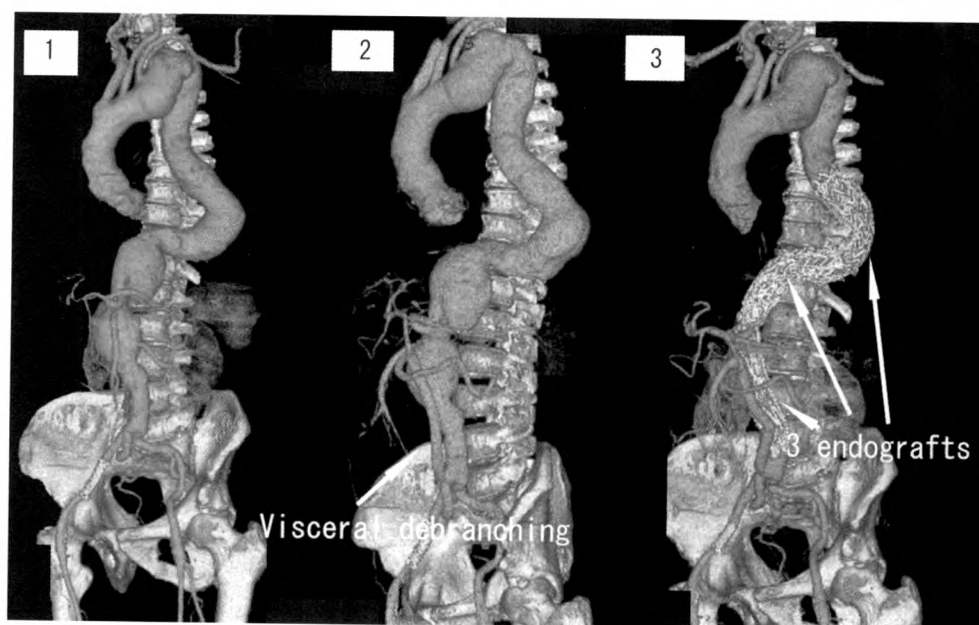


Fig. 1 A computed tomography (CT) 1 showed three dimensional reconstruction of patient's complex aortic pathology. A CT 2 showed patient's aorta after visceral debranching surgery. A CT 3 showed patient's aorta after endovascular surgery for thoraco-abdominal aortic aneurysm.

with Gianturco stent (William Cook Europe A/S, Bjæverskov, Denmark)) was performed (**Fig. 1**). We used a homemade stentgraft because the treatment length of this case was so long that we couldn't treat with two endografts, and the third commercial endograft could not be covered by insurance in Japan. The TEVAR procedure, combined with debranching of visceral branches under laparotomy, can be described as "hybrid" TEVAR. As protective measures of the spinal cord, perioperative intravenous infusion of naloxone (1 $\mu\text{g}/\text{kg}/\text{h}$) and continuous drainage of cerebrospinal fluid (CSF) to maintain intrathecal pressure not exceeding 10 cm H_2O , were carried out. Postoperative recovery was smooth without any neurological deficit. 2) Six months after hybrid TEVAR, open direct graft replacement of the segment between proximal ascending to distal arch aorta, using Triplex branched graft (Vascutek Terumo Ltd., Inchinnan, Scotland), was performed under a mid-sternal incision, with the use of cardiopulmonary bypass. Deep hypothermic circulatory arrest (23°C) with selective antegrade cerebral infusion was used to protect both cerebrum and spinal cord. An "elephant trunk" was hung down into somewhat enlarged proximal descending aorta. Postoperative recovery was uneventful. 3) Three months later, he transferred to our hospital by ambulance with severe back pain. A CT-scan image showed acute dissection of proximal descending aorta associated with cir-

cumferential pleural effusion, leading to the diagnosis of impending rupture (**Fig. 2**). An emergent TEVAR procedure of this aortic segment, bridging the elephant trunk of the arch graft and previous thoracoabdominal stentgraft with two Gore TAG endografts (28-mm $\times$ 15 cm and 34 mm $\times$ 20 cm), was performed (**Fig. 3**). Through all these phases, as a result, total aortic replacement was accomplished with combined open and TEVAR procedures successfully, without any neurological adverse events.

DISCUSSION

Since Dake, et al. first reported about TEVAR for descending thoracic aortic aneurysm in 1994,²⁾ growing demands as well as achievements of TEVAR have ever been expanding in these days. However, there still exists a controversy regarding application of this less invasive procedure for thoracoabdominal aneurysm. And while there are series of literature of direct total aortic replacement since the first successful report by Crawford et al.,³⁾ there are a few reports of extensive graft replacement using the TEVAR technique. For TEVAR of the thoracoabdominal aneurysm, we adopted the "hybrid" procedure, in which open debranching of major visceral branches with bypass grafting is combined with TEVAR procedure. According to the meta-analytic report of this

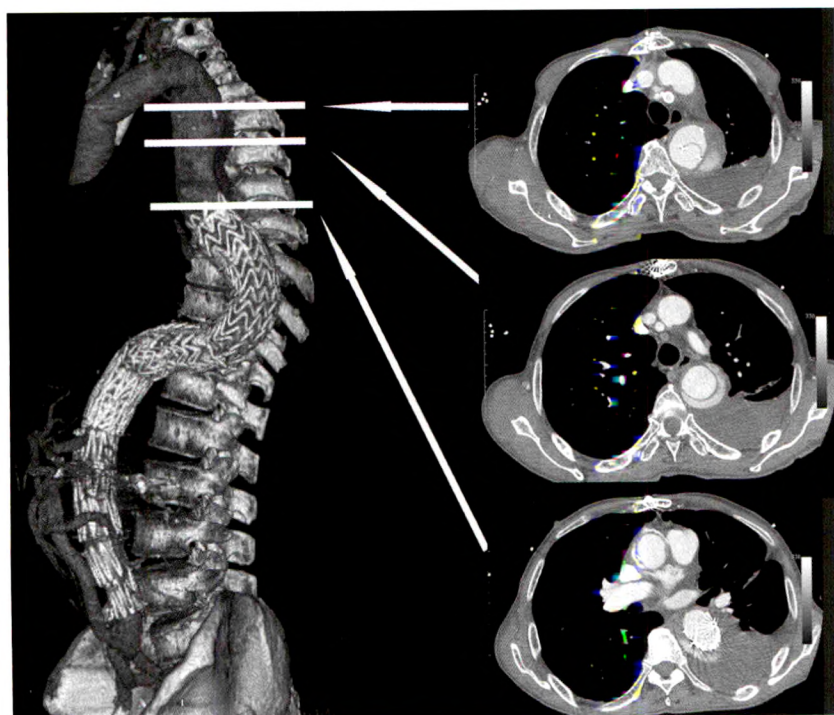


Fig. 2 A CT showed the impending ruptured aorta due to dissection of descending thoracic aorta 5 months after the patient being performed total arch replacement using elephant trunk technique.

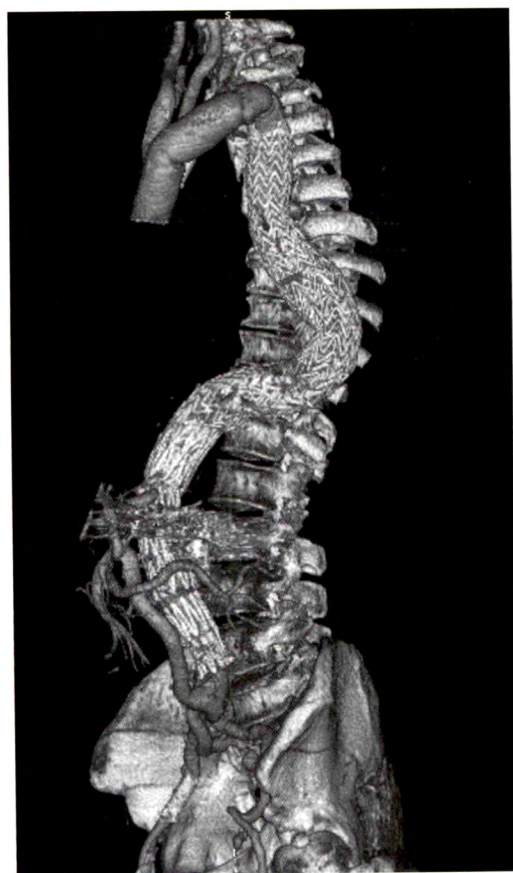


Fig. 3 A CT showed three dimensional reconstruction of patient's aorta after total aortic replacement from ascending aorta to bilateral common iliac artery.

hybrid procedure in various institutes where more than ten cases were performed, the result was not excellent with the mortality of 15%, paraplegia/paraparesis of 7% and renal failure rate of 9.9%.⁴⁾ However the result was still considerably better when compared with the average mortality of 20% and paraplegia/paraparesis rate of 16% in direct open graft replacement of thoracoabdominal aneurysms in the United States,¹⁾ although we realize that in high-volume, well experienced institute with expert surgeon(s) the result of open surgery can be as excellent as with the mortality of 7.3% and paraplegia rate of 4.6%.⁵⁾

We utilized the hybrid procedure this time for a 75 year-old patient with extensive aneurysm (Crawford type 2 with additional arch aneurysm) who had previous abdominal aortic replacement, a clinical setting known as most vulnerable to postoperative paraplegia.⁵⁾

As regards the visceral bypass grafts, the patency ratio has been reported to be good with 98%.⁴⁾ However as the bypass is non-anatomical, the long-term fate of it has to be thoroughly followed up. In this setting, experiences of the use of a fenestrated and branched stentgrafts in the TEVAR procedure have been reported, with considerably good results. Also this technique obviates the need of laparotomy, making all the procedure even less invasive. This time non-availability and lack of experience made us impossible to apply this technique, which

may seem promising and advantageous in the near future. As the protective measure of spinal cord from ischemia, we adopted the combined use of intravenous naloxone and continuous CSF drainage,⁶⁾ which seemed effective in preventing the occurrence of paraplegia/paraparesis.

Direct total arch replacement has been a well-established surgical method with low mortality and low stroke rate, which in the present case seemed preferable to the “open” stentgraft procedure, the latter reportedly with unexpected occurrence of postoperative paraplegia.⁷⁾ And we were not able to perform TEVAR with debranching because the size of ascending aorta was over 42 mm.

Occurrence of dissection relatively early after the TEVAR procedure in the proximal descending aorta deserves consideration. We think there may be a stress placed on the aortic intima in the area of the “flare” of the stentgraft, which could trigger the occurrence of wall damage and subsequent dissection. Although unreported, we have had a same experience of dissection after stentgraft deployment in the distal arch. In both cases emergency procedures successfully managed the situation (one in open surgery, one—present case—by additional TEVAR).

CONCLUSION

By using staged and combined open and TEVAR procedures, a successful total aortic replacement could be performed with no neurological adverse sequela nor any other complication. This less invasive method seems especially advantageous in old and compromised patients with extensive aneurysmal involvement.

DISCLOSURE STATEMENT

I declare that we have no ethical problem or conflict of interest in connection with this paper.

REFERENCES

- 1) Derrow AE, Seeger JM, Dame DA, et al. The outcome in the United States after thoracoabdominal aortic aneurysm repair, renal artery bypass, and mesenteric revascularization. *J Vasc Surg* 2001; **34**: 54-61.
- 2) Dake MD, Miller DC, Semba CP, et al. Transluminal placement of endovascular stent-grafts for the treatment of descending thoracic aortic aneurysms. *N Engl J Med* 1994; **331**: 1729-34.
- 3) Crawford ES, Coselli JS, Svensson LG, et al. Diffuse aneurysmal disease (chronic aortic dissection, Marfan, and mega aorta syndromes) and multiple aneurysm. Treatment by subtotal and total aortic replacement emphasizing the elephant trunk operation. *Ann Surg* 1990; **211**: 521-37.
- 4) Chiesa R, Tshomba Y, Melissano G, et al. Is hybrid procedure the best treatment option for thoraco-abdominal aortic aneurysm? *Eur J Vasc Endovasc Surg* 2009; **38**: 26-34.
- 5) Coselli JS, LeMaire SA, Miller CC 3rd, et al. Mortality and paraplegia after thoracoabdominal aortic aneurysm repair: a risk factor analysis. *Ann Thorac Surg* 2000; **69**: 409-14.
- 6) Acher CW, Wynn MM, Hoch JR, et al. Combined use of cerebral spinal fluid drainage and naloxone reduces the risk of paraplegia in thoracoabdominal aneurysm repair. *J Vasc Surg* 1994; **19**: 236-46; discussion 247-8.
- 7) Yamada K, Mochizuki T, Tsubota H, et al. Early and midterm outcomes of open stent-graft treatment for distal aortic arch aneurysm. *Gen Thorac Cardiovasc Surg* 2008; **56**: 490-7 Epub 2008 Oct 15.

» Case Report «

Emergent Thoracic Endovascular Aortic Repair for Acute Type-B Aortic Dissection with Malperfusion by Matsui-Kitamura Stent Graft

Yuji Nishida, MD,¹ Hiroshi Ohtake, MD,¹ Ryuta Kiuchi, MD,¹ Junichirou Sanada, MD,² Osamu Matsui, MD,² and Go Watanabe, MD¹

Acute type-B aortic dissection with malperfusion is a serious cardiovascular condition associated with high morbidity and mortality. Recent studies have investigated the efficacy of thoracic endovascular aortic repair (TEVAR) as treatment for acute aortic dissection. In this report, we present a case of acute type-B aortic dissection complicated with malperfusion, which was successfully treated with emergent TEVAR for entry closure by a Matsui-Kitamura stent graft (MKSG). MKSG is a flexible custom-made curved stent graft. The main advantages of MKSG for emergent TEVAR include flexibility, shape, and small profile when compressed.

Keywords: TEVAR, malperfusion, Matsui-Kitamura stent graft

INTRODUCTION

Approximately 30% of patients with aortic dissection develop organ malperfusion, and the prevalence of visceral organ malperfusion is closely related with surgical mortality and morbidity, ranging from 50% to 80%.¹⁾ Surgical intervention is necessary to improve the chance of survival and to reduce the severity of this condition among survivors. As compared to open surgical repair, the endovascular repair for emergency thoracic aortic dissection has a lower mortality rate (31.5% and 12%, respectively).^{2, 3)} In this report, we present a case of acute Stanford type B thoracic aortic dissection complicated with malperfusion, which was successfully treated with emergent thoracic endovascular aortic repair (TEVAR)

for entry closure by Matsui-Kitamura stent graft (MKSG).

CASE REPORT

A 53 year-old man was admitted to our hospital because of back pain. He had a history of a poorly controlled hypertension with no history of collagen vascular disorders. Severe hypertension (185/77 mmHg in the right arm and 156/59 in the left arm) was observed on admission. Both the femoral arteries were palpable, and physical examination of the chest and abdomen showed no signs of visceral ischemia. Laboratory data indicated the elevation of white blood cell count (19770/mm³) and serum creatinine (1.62 mg/dL). Contrast enhanced computer tomography (CT) revealed an acute type-B aortic dissection extending from the descending aorta to the right common iliac artery. There was a relative severe stenosis of the true lumen at the descending thoracic aorta because of the dynamic obstruction caused by the extended false lumen. Blood to the celiac, superior mesenteric, and both the renal arteries was supplied from the true lumen (**Fig. 1**). Conservative therapy was started because he had no ischemic complain. Five hours after admission, he suddenly developed right leg pain. The laboratory data revealed progressive acidosis with pH, 7.310 and elevation

¹Departments of General and Cardiothoracic Surgery, Kanazawa University, Kanazawa, Ishikawa, Japan

²Departments of Radiology, Kanazawa University, Kanazawa, Ishikawa, Japan

Received: June 29, 2011; Accepted: September 12, 2011
Corresponding author: Yuji Nishida, MD. Departments of General and Cardiothoracic Surgery, Kanazawa University, Takaramachi 13-1, Kanazawa, Ishikawa 920-8641, Japan
Tel: +81-76-235-2355, Fax: +76-222-6833
E-mail: yu-ji@umin.net

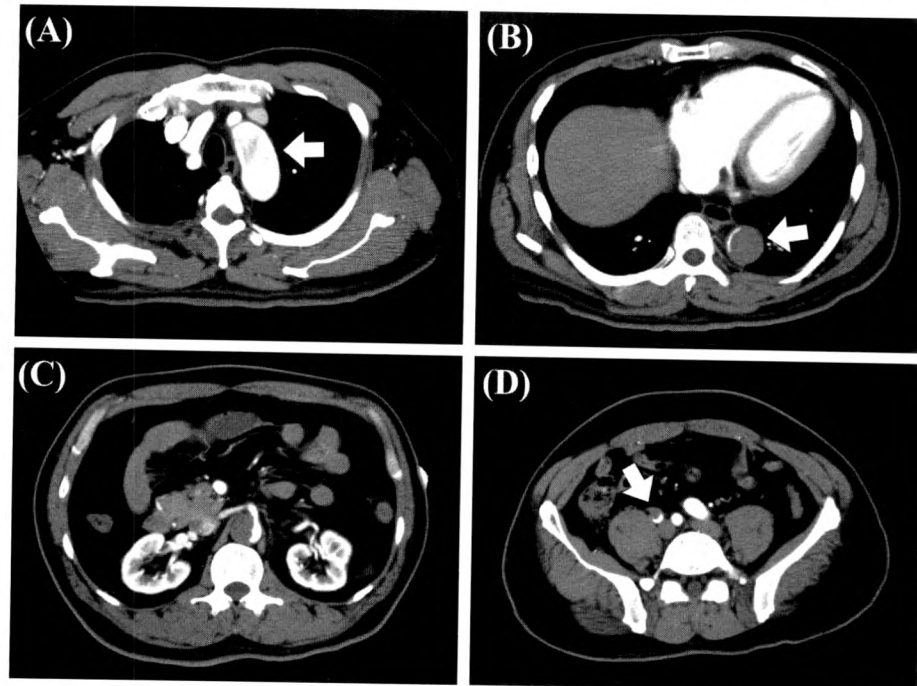


Fig. 1 Preoperative enhanced CT (Axial images).

A: Upper thoracic level. *Arrow* shows the intimal tear.

B: Lower thoracic level. *Arrow* shows a severe stenosis of the true lumen by dynamic obstruction.

C: Upper abdominal level.

D: Lower abdominal level. *Arrow* shows the dissection extending to the right common iliac artery.

of serum lactate to 4.6 mmol/L. For this malperfusion of lower extremities, emergent TEVAR for an entry closure was planned. General anesthesia was administered, and the left femoral artery was exposed. By intra-vascular ultrasound (IVUS), a guide-wire was introduced to the true lumen. Preoperative angiography showed severe stenosis of the true lumen and entry of the descending thoracic aorta. An MKSG that was 30-mm diameter and 115-mm-length curved was delivered through an 18-Fr sheath. The deployment was successfully performed, and the entry was occluded. To achieve enough proximal landing zone, the left subclavian artery was sacrificed (**Fig. 2**). After the operation, there were no ischemic symptoms of the cerebral, abdominal organs, bilateral legs, or arms. One month after TEVAR, postoperative CT showed no migration of the MKSG or progression of the thrombosis in the false lumen at the descending thoracic aorta (**Fig. 3**).

DISCUSSION

There is a consensus that medical treatment is better

than surgery for uncomplicated acute type B aortic dissection.⁴⁾ The International Registry of Acute Aortic Dissection (IRAD) investigators have previously reported a hospital mortality rate of 32% for patients treated by open surgical repair, 7% for patients managed by TEVAR, and 10% for those who underwent conservative medical therapy alone.⁵⁾ However, patients with acute type B aortic dissection complicated by malperfusion or rupture constitute a very high-risk subset. Emergency treatment options include open surgical thoracic aortic graft replacement, interventional or surgical flap fenestration and true lumen stenting, catheter reperfusion or extra-anatomic surgical bypass, or TEVAR.

Minimally invasive approaches such as TEVAR are an attractive option for acute type B aortic dissection patients; however, severe device-related complications can nonetheless occur in these procedures. The complications of the endoluminal approach, including a secondary intimal tear as a result of the stent wires, retrograde type A aortic dissection, endoleaks, late reperfusion of the false lumen and arterial injury at the site of access, have been occasionally observed. Since these complications

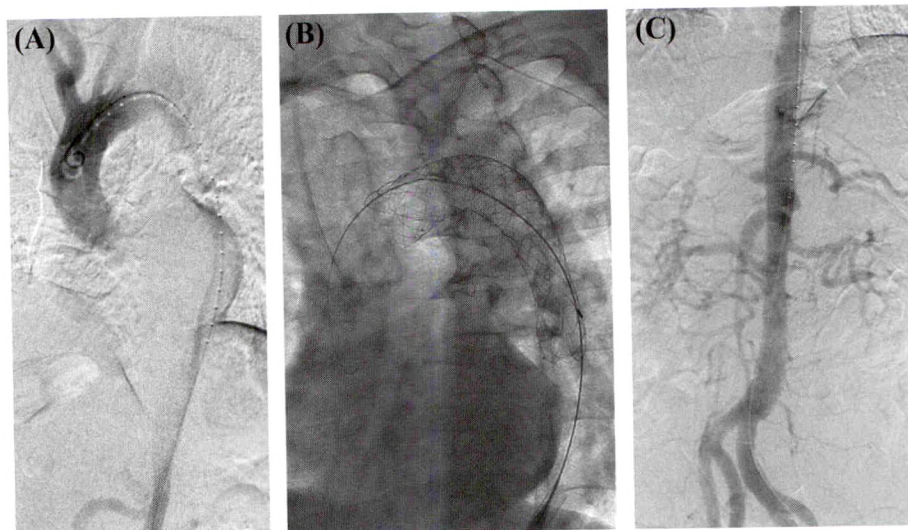


Fig. 2 Intraoperative digital subtraction angiography (DSA) images.
A: Pre-deployment image. There was the entry tear at the distal site of left subclavian artery, and the dynamic obstruction of the true lumen.
B: Post-deployment image of the thoracic aorta.
C: Post-deployment image of the abdominal aorta.

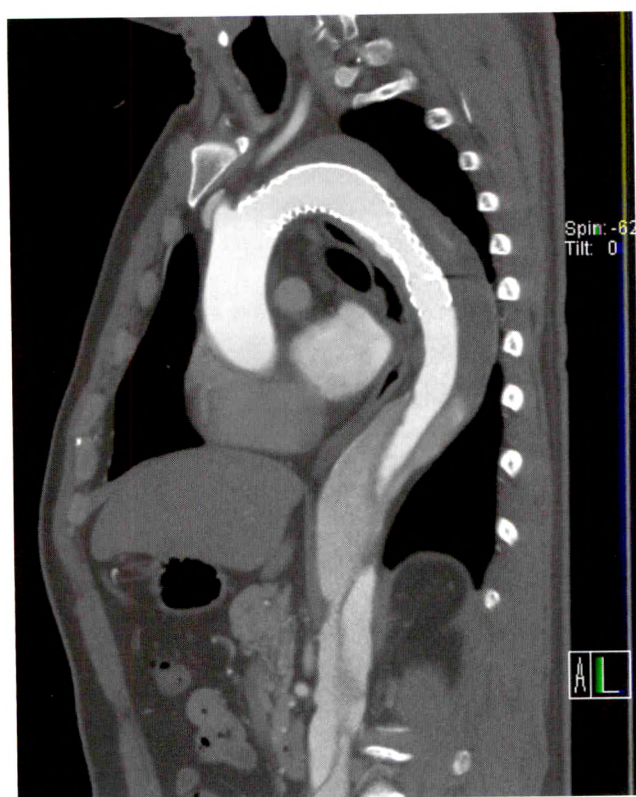


Fig. 3 Postoperative CT (Multi planar reconstruction image).

can occur early or late after TEVAR, stringent follow-up imaging is recommended in all patients with additional re-interventions as required.^{6, 7)} In Japan, two commer-

cially available devices (GORE® TAG®, Medtronic TAL-ENT®) are commonly used for the follow up of these patients. However, these devices are not recommended for acute type B dissection patients. The edge of these commercially stent grafts is too hard for the fragile intima of acute aortic dissection.

The MKSG is a flexible custom-made stent graft.⁸⁾ The MK stent is made by using super-elastic nitinol wire 0.3–0.4 mm in diameter. The advantage for this ultra-flexible stent grafting technique is its ease of delivery and the gentleness for the fragile intima. The curved configuration of the MKSG accommodated into the aortic arch shape which reduced a late deformation or migration of the stent graft, thereby preventing the occurrence of an endoleak and minimizing injury to the intima.

The main cause of failure in the use of TEVAR for acute dissection is damage to the intima and access route caused by the device,⁹⁾ which occurs in 3%–15% of patients.¹⁰⁾ In general, commercially available stent graft repair requires a 20- to 24-F system, but the MKSG with < 36 mm diameter were deployed through an 18-F sheath. Because 18-F system was induced via the femoral artery without arterial cross-clamping, we could set the active coagulation time at a maximum of 180 to 200 s and prevent hemorrhage as much as possible.

In conclusion, a good result was obtained by using a curved MKSG for complicated, acute type-B aortic

dissection. The main advantages of MKSG for emergent TEVAR include its flexibility, shape memory, and small profile compared with commercially available devices. Further, we are planning a strict, long term follow-up for this patient.

REFERENCES

- 1) Vedantham S, Picus D, Sanchez LA, et al. Percutaneous management of ischemic complications in patients with type-B aortic dissection. *J Vasc Interv Radiol* 2003; **14**: 181-94.
- 2) Tefera G, Acher CW, Hoch JR, et al. Effectiveness of intensive medical therapy in type B aortic dissection: a single-center experience. *J Vasc Surg* 2007; **45**: 1114-8; discussion 1118-9.
- 3) Leurs LJ, Bell R, Degrieck Y, et al. Endovascular treatment of thoracic aortic diseases: combined experience from the EUROSTAR and United Kingdom Thoracic Endograft registries. *J Vasc Surg* 2004; **40**: 670-9; discussion 679-80.
- 4) Dake MD, Kato N, Mitchell RS, et al. Endovascular stent-graft placement for the treatment of acute aortic dissection. *N Engl J Med* 1999; **340**: 1546-52.
- 5) Suzuki T, Mehta RH, Ince H, et al. Clinical profiles and outcomes of acute type B aortic dissection in the current era: lessons from the International Registry of Aortic Dissection (IRAD). *Circulation* 2003; **108**: II312-7.
- 6) Girdauskas E, Falk V, Kuntze T, et al. Secondary surgical procedures after endovascular stent grafting of the thoracic aorta: successful approaches to a challenging clinical problem. *J Thorac Cardiovasc Surg* 2008; **136**: 1289-94 Epub 2008 Aug 29.
- 7) Dong ZH, Fu WG, Wang YQ, et al. Retrograde type A aortic dissection after endovascular stent graft placement for treatment of type B dissection. *Circulation* 2009; **119**: 735-41 Epub 2009 Jan 26.
- 8) Sanada J, Matsui O, Terayama N, et al. Clinical application of a curved nitinol stent-graft for thoracic aortic aneurysms. *J Endovasc Ther* 2003; **10**: 20-8.
- 9) Makaroun MS, Dillavou ED, Kee ST, et al. Endovascular treatment of thoracic aortic aneurysms: results of the phase II multicenter trial of the GORE TAG thoracic endoprosthesis. *J Vasc Surg* 2005; **41**: 1-9.
- 10) Zipfel B, Hammerschmidt R, Krabatsch T, et al. Stent-grafting of the thoracic aorta by the cardiothoracic surgeon. *Ann Thorac Surg* 2007; **83**: 441-8; discussion 448-9.

» Case Report «

Conservative Therapy for Surgically Untreatable Extensive Arteriovenous Malformation from the Lower Extremity to the Pelvis with Secondary Consumptive Coagulopathy

Yoshiko Watanabe, MD, PhD, Toru Iwashashi, MD, PhD, Naozumi Saiki, MD, Nobusato Koizumi, MD, PhD, Toshiya Nishibe, MD, PhD, and Hitoshi Ogino, MD, PhD

We present a woman with surgically untreatable extended arteriovenous malformations (AVM) and consumptive coagulopathy, which had been controlled by conservative compression and anticoagulation therapies for 17 years. At age 13, she was diagnosed with extended AVM in the entire left leg and pelvis. At age 16, limited surgical resection of the enlarged superficial vein in the left calf was performed for persistent leg pain. One year later, anticoagulation therapy was performed for massive bleeding from hemorrhoids due to AVM and coagulopathy. Despite its intractability, her condition has been favorably controlled with conservative methods, including compression and anticoagulation therapies.

Keywords: arteriovenous malformation, vascular malformation, consumptive coagulopathy

INTRODUCTION

Extensive vascular malformations are rare and are occasionally associated with chronic coagulopathy caused by localized intravascular coagulation (LIC), especially in predominantly venous malformations.^{1, 2)} Not only the prognosis, but also the treatment methods for vascular malformations vary according to the particular lesions of each patient.³⁾ We report a woman with extended lesions of arteriovenous malformation (AVM) in the entire left lower extremity and the interior of the pelvis, associated with serious consumptive coagulopathy, who has been successfully followed up for 17 years with favorable control achieved by conservative methods, including compression and anticoagulation therapies.

*Department of Vascular Surgery, Tokyo Medical University,
6-7-1 Nishishinjuku, Shinjuku-ku, Tokyo 160-0023, Japan*

Received: July 21, 2011; Accepted: September 23, 2011
Corresponding author: Yoshiko Watanabe, MD, Department of
Vascular Surgery, Tokyo Medical University, 6-7-1 Nishishin-
juku, Shinjuku-ku, Tokyo 160-0023, Japan
Tel: +81-3-3342-6111, Fax: +81-3-3342-6193
E-mail: yosiyosi515@mac.com

CASE

A 30 year-old woman, with a thickened left lower extremity and enlarged superficial veins, was initially diagnosed with hemangioma at the age of 13. She was referred to our institution due to exacerbation of her long standing leg pain as she grew. No evidence of nevus was recognized, and her lower extremities were equal in length, but she had chronic anemia caused by bleeding from internal hemorrhoids. Intravenous digital subtraction angiography (IV-DSA) showed abnormal connections between the arteries and veins in her left thigh with enlargement of her internal iliac veins. However, she did not return to hospital until the age of 16, when she presented with recurrence of her leg pain. Her laboratory data revealed consumption coagulopathy as follows: platelet count, 130×10^3 /ml, serum fibrinogen level, 125 mg/dl, fibrin degradation products (FDP) 615 mg/dl, and D-dimer level, 8.23 μ g/dl. Because the lesions in the left thigh were too extensive to be treated surgically, limited surgical resection of the enlarged superficial vein in the left calf only was performed to improve her stasis pain. In the operative findings, the veins had many branches connecting to the subfascial layer in the popliteal region. The pathological findings of the popliteal side

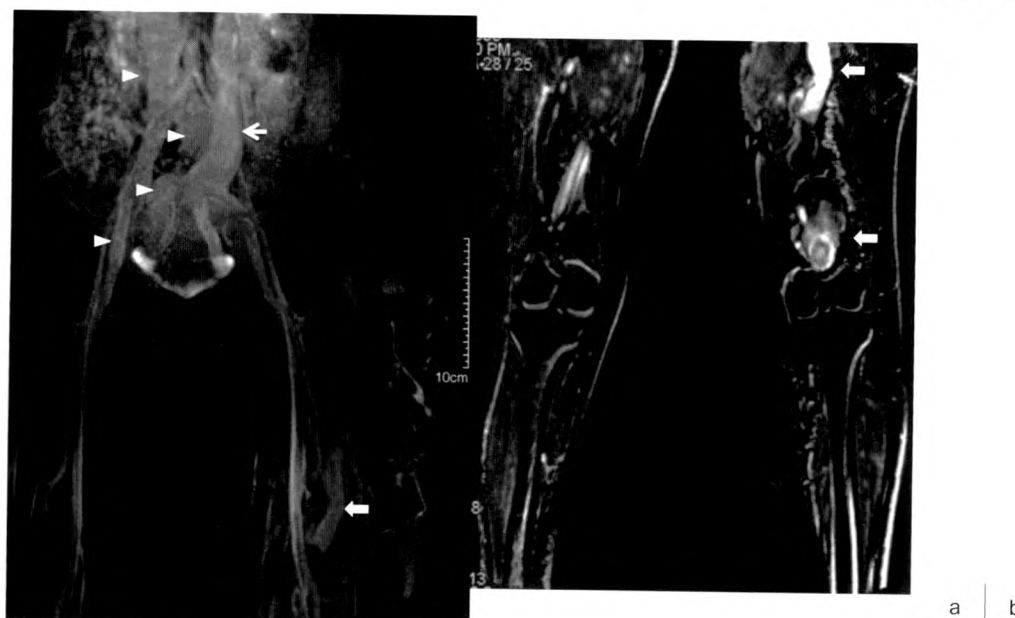


Fig. 1 Magnetic resonance (MR) venographic image of the pelvis and lower extremities
a: Pelvis and thighs show a dilated ischiatic vein (bold arrow) and numerous low-flow vessels subcutaneously in the external side of the enlarged left thigh and hip. The bilateral internal iliac veins, the bilateral external veins, and the IVC are dilated. A thin arrow indicates an abnormal vein which branches from the internal iliac veins and connects to the SMA.
b: The lower extremities. The dilated left ischiatic vein was partially obstructed by a thrombus (thick arrows).

of the resected veins showed well-developed smooth muscles in the media, which resembled the arterial findings. The veins also had anastomosing vessels; therefore, AVM was subsequently diagnosed. However, her secondary consumption coagulopathy markedly deteriorated after surgical intervention, showing a serum fibrinogen level of 85 mg/dl and an FDP of 2040 mg/dl. Unfortunately, her condition was not improved by the administration of tranexamic acid. In addition, because her pain due to blood stasis in the left leg was slightly improved but still remained, we employed conventional compression therapy with an elastic bandage.

At age 17, massive bleeding from the internal hemorrhoids occurred due to the AVM in the pelvis and secondary consumption coagulopathy. She presented in a state of shock and was initially given a blood transfusion. We then gave her anticoagulation therapy with warfarin for the consumption coagulopathy, which had worsened. Thereafter, she came regularly to the hospital to receive prescriptions until the age of 24.

After an interval of 2 years, at age 26, she again returned to hospital, while pregnant and with complaints of bleeding from hemorrhoids. Her consumptive coagu-

lopathy got worse. Warfarin is teratogenic, and moreover, she did not wish to remain pregnant. In addition, it was considered that bleeding from hemorrhoids would worsen as her pregnancy progressed. Eventually, she elected to abort the pregnancy and started taking warfarin again. Magnetic resonance imaging (MRI) of the pelvis and the lower extremities (**Fig. 1**) showed numerous vessels between the muscles at the posterior of the entire left lower extremity. The thickened left ischiatic vein was partially obstructed by a thrombus, but the branches of the bilateral internal iliac veins could be seen. The lateral external aspect along the left thigh from the left hip was enlarged, and there were numerous low-flow vessels subcutaneously connecting the left femoral vein and the veins in the gluteal muscle and iliopsoas muscle. Neither AVF nor an obvious feeding artery was found. She did not have any evidence of heart failure, nor did ultrasonic cardiography show any signs of right heart strain.

The superficial varices on her left hip slowly grew. At the age of 27, a small stasis ulcer developed on this hip. Enhanced computed tomography (CT) showed enlargement of the bilateral internal iliac veins and inferior vena cava (IVC) (**Fig. 2**). Enlarged small arteries were



Fig. 2 Enhanced computed tomographic (CT) images from the abdomen to the pelvis. The patient received 100 mL of iodinated contrast media, which was administered intravenously at a rate of 3 mL/sec. Imaging was performed 30 sec after the initiation of intravenous contrast material administration. (a–c) CT images show an abnormal vein which branched from the internal iliac vein and connected to the SMA, and which was strongly enhanced in the early phase (thin arrows). The common iliac artery and the IVC were dilated (bold arrows). (d) The branches of the internal iliac vein are dilated. Numerous vessels can be seen in the enlarged left-side hip subcutaneously. Although an artery can be seen in the left hip (arrowhead), no obvious feeding artery was detected around the varices on the left hip.



Fig. 3 A photograph of the lower extremities at age 30. The left lower extremity and hip are enlarged and deformed.

recognized around the ascending colon, and the internal iliac veins and superior mesenteric vein (SMV) were strongly enhanced in the early phase (30 sec after the initiation of intravenous contrast material administration), which suggested the presence of AVM. The enlarged branch of the right internal iliac vein formed a venous arcade around the pancreatic body connected to the SMV. The portal vein was also enlarged, although the hepatic veins connecting to the IVC were not enlarged. No obvious feeding arteries were detected around the varices on the left hip. Her laboratory data did not show any hepatic dysfunction. Compression therapy by an adjusted girdle was increased, and local sclerotherapy using 1% polidocanol by direct injection to the varices on the hip was performed. Subsequently, the ulcer rapidly healed.

At age 30, MRI showed no remarkable changes in the abdomen and pelvis, except for a slight spreading of varices on the left hip. Her subsequent course was uneventful, since the condition was favorably controlled with local compression and anticoagulation therapies.

Her latest laboratory data were as follows: platelet count, 111×10^3 /ml; serum fibrinogen level, 190 mg/dl; and D-dimer level, 2.51 μ g/dl (**Fig. 3**).

DISCUSSION

Congenital hemangiomas are vascular tumors in infants and children that are characterized by a growth phase and an involution phase. Arteriovenous fistulas are acquired abnormal connections between arterial and venous systems, bypassing the normal anatomic capillary beds. In contrast, AVM is a congenital abnormal connection between arterial and venous systems mediated by abnormal capillaries (a nidus). AVMs present at birth deteriorate slowly with age.³⁾

With regard to surgical treatment, Eifert et al. reported that anomalies of the deep vein system occur in almost half of venous malformations; phlebectasias occur in over one-third of cases, and aplasia/hypoplasia occurs in less than 10%.⁴⁾ Excision of the enlarged superficial compensatory varices may be deleterious if there is aplasia or

hypoplasia of deep vein system trunks. Consequently, in this case, we chose to perform limited surgical excision of the superficial varices only on the left calf because the deep vein system was patent.

More invasive treatments might be required for patients with vascular malformation if they have uncontrollable pain, clinically significant heart strain, intractable ulcer, functional disorder, or disfigurement. Either complete resection or occlusion of the nidus is required for complete cure of AVM. Imperfect embolization of the feeder arteries does not reduce the nidus and exacerbate the condition due to the development of collateral vessels. Sclerotherapy for venous malformation, if extensive, can result in serious deformation, damage or a skin ulcer. Therefore, in many cases, the aim of treatment for vascular malformation is for symptomatic relief rather than a cure.⁵⁻⁷⁾ Before invasive treatment for vascular malformations, detailed imaging diagnostic procedures such as catheter angiography are required. Because the symptoms of this patient were controlled conservatively, she did not need to undergo further invasive examination or intervention.

Extensive venous malformations are occasionally associated with chronic coagulopathy, which can result in confusion with Kasabach-Merritt syndrome. However, Kasabach-Merritt syndrome is a congenital hemangioma with disseminated intravascular clotting in children and is a different condition from vascular malformations with coagulopathy.¹⁾ In the present case, the lesions developed very slowly as the patient grew, and she had no sign of right heart strain or mild symptoms of venous stasis, therefore, her disease was first considered being AVM with a small shunt volume. However, she had extensive venous enlargement which developed into serious consumptive coagulopathy due to a mechanism similar to that of venous-predominant vascular malformation. Her consumptive coagulopathy showed a normal amount or mild decrease in her platelet counts, but there was a decrease in her serum fibrinogen level and an increase in her D-dimer level and FDPs, findings characteristic of LIC associated with venous malformation. Mazoyer et

al. reported that a vitamin K antagonist was ineffective and advocated that permanent elastic compression with heparin therapy was the only effective treatment for LIC.¹⁾ However, the present patient's coagulopathy improved and has been well controlled by only warfarin therapy and compression. Nevertheless, careful follow-up of possible stasis complications and coagulation disorder will be required for some time in the future.

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REFERENCES

- 1) Mazoyer E, Enjolras O, Laurian C, et al. Coagulation abnormalities associated with extensive venous malformations of the limbs: differentiation from Kasabach-Merritt syndrome. *Clin Lab Haematol* 2002; **24**: 243-51.
- 2) Enjolras O, Ciabrini D, Mazoyer E, et al. Extensive pure venous malformations in the upper or lower limb: a review of 27 cases. *J Am Acad Dermatol* 1997; **36**: 219-25.
- 3) Lee BB. Changing concept on vascular malformation: No longer enigma. *Ann Vasc Dis* 2008; **1**: 11-9.
- 4) Eifert S, Villavicencio JL, Kao TC, et al. Prevalence of deep venous anomalies in congenital vascular malformations of venous predominance. *J Vasc Surg* 2000; **31**: 462-71.
- 5) Goyal M, Causer PA, Armstrong D. Venous vascular malformations in pediatric patients: comparison of results of alcohol sclerotherapy with proposed MR imaging classification. *Radiology* 2002; **223**: 639-44.
- 6) Lee BB, Kim DI, Huh S, et al. New experiences with absolute ethanol sclerotherapy in the management of a complex form of congenital venous malformation. *J Vasc Surg* 2001; **33**: 764-72.
- 7) Lee BB, Do YS, Yakes W, et al. Management of arteriovenous malformations: a multidisciplinary approach. *J Vasc Surg* 2004; **39**: 590-600.

» Case Report «

Surgical Treatment for Aortic Coarctation with Chronic Type B Dissection: Report of a Case

Yohsuke Yanase, MD, Nobuyoshi Kawaharada, MD, PhD, Takayuki Hagiwara, MD, Junji Nakazawa, MD, Toshiyuki Maeda, MD, Tetsuya Koyanagi, MD, Toshiro Ito, MD, PhD, Yoshihiko Kurimoto, MD, PhD, and Tetsuya Higami, MD, PhD

The aim of this paper is to report a rare case of aortic coarctation with type B aortic dissection. A 37 year-old man had sudden, intense back pain. Enhanced computed tomography revealed aortic coarctation (CoA) at the proximal descending aorta and acute type B aortic dissection just distal to the CoA. The dissecting, descending aortic aneurysm had expanded to a maximal diameter of 52 mm. The aortic coarctation was resected and then the descending aorta was replaced with prosthetic grafts in an uneventful procedure. Surgical repair resulted in a good outcome.

Keywords: aortic dissection, aortic coarctation, thoracic aorta

INTRODUCTION

Aortic coarctation (CoA) is usually diagnosed and treated in childhood. We describe a rare aortic coarctation with Stanford type B dissection in an adult who was surgically treated by an unusual approach.

CASE REPORT

A 37 year-old man suddenly developed intense back pain and rushed to his local hospital where enhanced computed tomography (CT) revealed acute type B aortic dissection. Stenosis in the proximal descending aorta was diagnosed as CoA. He was treated with strict blood pressure control. However, 2 years later, the dissecting descending aorta was expanded to a maximal diameter of 52 mm. He was referred to our department for further

evaluation. He had a history of hypertension and had been treated with an antihypertensive agent. A physical examination revealed the following: body weight, 58.0 kg; height, 167 cm; blood pressure, 139/72 and 132/72 mmHg in the right and left upper extremities, respectively, and 104/71 and 98/69 mmHg in the right and left lower extremities, respectively. The right and left ankle brachial indexes (ABI) were 0.77 and 0.72, respectively, which indicated a pressure gradient between the upper and lower extremities. The results of blood tests were all within normal ranges. Spirography revealed vital capacity, 4.09 g/L; %VC, 105%; FEV1.0, 3.48 L and FEV1.0%, 85%, indicating the absence of a respiratory disorder. Three-dimensional computed tomography (3D-CT) showed CoA of the proximal descending aorta (**Fig. 1**). Aortic dissection extended from a point just distal to the CoA as far as the terminal abdominal aorta. A dissecting aortic aneurysm had expanded to a maximal diameter of 52 mm. The branching level of the Adamkiewicz artery was right Th10 segmental artery. The innominate vein crossed the anterior side of the distal arch aorta and the dorsal side of the ascending aorta. Since the proximal descending aorta was closely located to the first costal bone, we considered that the surgical view obtained by posterolateral thoracotomy would be insufficient. We decided to approach via a median sternotomy and anterolateral thoracotomy with the patient

Department of Thoracic and Cardiovascular Surgery, Sapporo Medical School of Medicine, Sapporo, Hokkaido, Japan

Received: July 31, 2011; Accepted: September 23, 2011
Corresponding author: Yohsuke Yanase, MD, Department of Thoracic and Cardiovascular Surgery, Sapporo Medical University of Medicine, South 1, West 16, Chuo-ku, Sapporo, Hokkaido 060-8543, Japan
Tel: +81-011-611-2111, Fax: +81-011-621-8059
E-mail: yanasey@sapmed.ac.jp

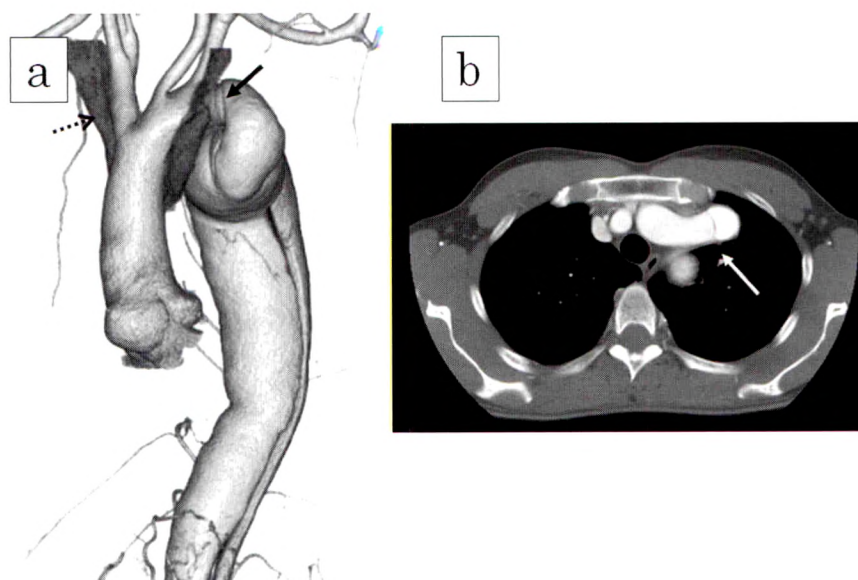


Fig. 1 Preoperative enhanced computed tomography.
a: Aortic coarctation (black arrow) and Stanford type B aortic dissection. The innominate vein (dotted arrow) crossed the anterior side of the distal arch aorta and the dorsal side of the ascending aorta.
b: Distal aortic arch is located close to first costal bone (white arrow), which complicated proximal anastomosis approached via posterolateral thoracotomy.

in the right half-spine position with an elevated left arm. The patient was intubated under general anesthesia with a double lumen tube. At first, the surgical bed was rotated 45 degrees to the left. In this position, a cardiopulmonary bypass was established via the right axillary artery and superior vena cava and inferior vena cava cannulated via a femoral vein. Then, the surgical bed was rotated to flat, and antero-lateral thoracotomy was begun in the fourth costal space. The surgical view was sufficient, and the aneurysm was easily exposed. While the patient was under deep hypothermic, circulatory arrest, we resected the CoA and anastomosed a 20-mm prosthetic graft to the proximal descending aorta by the open proximal technique. A fenestration was created at the level of Th 9, just distal of anastomosis site of the descending aorta, and a 26-mm prosthetic graft was anastomosed using the open distal technique. The body temperature was recovered, and each prosthetic graft was anastomosed. The durations of surgery, cardiopulmonary bypass, and circulatory arrest were 495, 156, and 29 minutes, respectively. The patient was placed in the intensive care unit. His respiratory status was satisfactory, and he was extubated on postoperative day 1. Postoperative enhanced CT showed no pseudoaneurysms at the anastomosis sites (Fig. 2). The postoperative ABI improved to values of 0.98 and 1.03 for the right and left, respectively. The postoperative course was uneventful, and

he was discharged on postoperative day 26.

DISCUSSION

Aortic coarctation is rare in adults and remains asymptomatic in 69% of such patients.¹⁾ Aortic coarctation was incidentally discovered in our patient during an enhanced CT to determine the cause of the sudden back pain. Together with type A aortic dissection, CoA is often discovered in Turner syndrome.²⁾ Major causes of dissection in patients with coarctation are hypertension of the upper body and ascending aortic dilatation. However, type B aortic dissection with CoA is unlikely because blood pressure decreases distal to the CoA, and arterial wall tension is reduced. Type B aortic dissection usually arises after angioplasty, or during post surgical treatment,³⁾ and it rarely arises spontaneously. To our knowledge, 9 reports were available worldwide.^{4–12)} An indication for surgery for Type B dissection associated with coarctation is not unknown. But in our case, the dissecting, aortic aneurysm, expanded to over a 50-mm diameter and had grown rapidly. So we thought the aneurysm was at risk of rupture.

The standard approach to CoA is via posterolateral thoracotomy at the fourth intercostal space. However, to anastomose the proximal descending aorta via posterolateral thoracotomy was difficult in our patient due to the

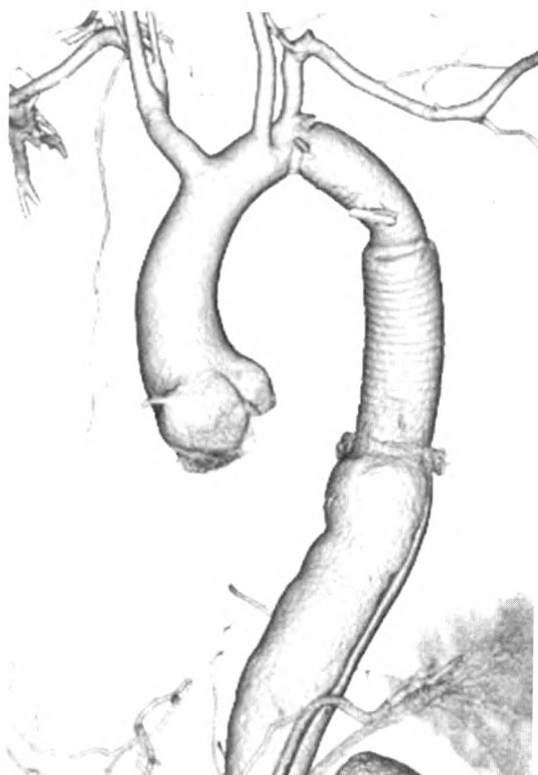


Fig. 2 Postoperative enhanced computed tomography. The Picture showed no pseudoaneurysms at the anastomosis sites. Descending aorta was replaced from distal of left subclavian artery to at the level of Th 9.

anatomical position of the aorta. We thus selected a median full sternotomy with an anterolateral thoracotomy (open door). The aortic arch and aneurysm was easily exposed using this approach, which has also been applied by Milano et al.⁷⁾ Although this approach offers a good view from the aortic arch to the descending aorta, it is invasive and can cause respiratory failure.¹³⁾ On the other hand, Ohata described that a median sternotomy with a left anterolateral thoracotomy does not increase postoperative respiratory complications.¹⁴⁾ Our patient was smoothly extubated, and respiratory failure did not arise.

In the anastomosis of the proximal descending aorta, we selected the open proximal technique because of the fragility of the aortic wall and clumping of the aorta, a risk of the new dissection. So we performed open proximal anastomosis under deep hypothermia with circulatory arrest.

CONCLUSION

We surgically treated a rare aortic coarctation with Stanford type B aortic dissection in an adult using a

median full sternotomy with an anterolateral thoracotomy. The postoperative course was uneventful, and the outcome was good.

CONFLICT OF INTEREST STATEMENT

None of the authors declares any conflict of interest.

REFERENCES

- 1) Bouchart F, Dubar A, Tabley A, et al. Coarctation of the aorta in adults: surgical results and long-term follow-up. *Ann Thorac Surg* 2000; **70**: 1483-8, discussion 1488-9.
- 2) Bondy CA. Aortic dissection in Turner syndrome. *Curr Opin Cardiol* 2008; **23**: 519-26.
- 3) Beitzke A, Stein JI, Gamillscheg A, et al. Dissection of the descending aorta after balloon angioplasty of native coarctation. *Pediatr Cardiol* 1997; **18**: 222-5.
- 4) Shin JS, Sun K, Shim WJ, et al. Acute descending aortic dissection associated with coarctation in adult. *Asian Cardiovasc Thorac Ann* 2002; **10**: 354-5.
- 5) Yamaguchi A, Adachi H, Kamio H, et al. A combination of preductal aortic coarctation and type B dissection: report of a case. *Surg Today* 1998; **28**: 435-7.
- 6) Kato W, Ueda Y, Akihiko U, et al. Type B aortic dissection associated with coarctation of the aorta. *Gen Thorac Cardiovasc Surg* 2007; **55**: 302-4.
- 7) Liu YC, Liu KS, Huang YK, et al. Adult coarctation of aorta presenting as aortic dissection. *Asian Cardiovasc Thorac Ann* 2010; **18**: 311.
- 8) Kreitmair P, Schmitt R, Jourdan J, et al. Aneurysms complicating coarctation of the aorta: anatomic aspects and evolution. Report of six successful surgical cases. *Thorac Cardiovasc Surg* 1982; **30**: 315-8.
- 9) Bhan A, Agarwal S, Sharma R, et al. Juxtaductal coarctation with type B dissection of the aorta: a new operative technique. *J Thorac Cardiovasc Surg* 2002; **123**: 365-7.
- 10) Katsumata T, Westaby S. Operation of mid-arch coarctation. *Ann Thorac Surg* 1999; **67**: 1386-90.
- 11) Graeter T, Schaefer C, Prokop M, et al. Three-dimensional vascular imaging—an additional diagnostic tool. *Thorac Cardiovasc Surg* 1993; **41**: 183-5.
- 12) Milano A, De Carlo M, Gigoni R, et al. Acute type-B aortic dissection in association with isthmic coarctation. *Tex Heart Inst J* 2001; **28**: 152-3.
- 13) Yamashiro S, Kuniyoshi Y, Arakaki K, et al. Aortic replacement via median sternotomy with left anterolateral thoracotomy. *Asian Cardiovasc Thorac Ann* 2009; **17**: 373-7.
- 14) Ohata T, Sakakibara T, Takano H, et al. Total arch replacement for thoracic aortic aneurysm via median sternotomy with or without left anterolateral thoracotomy. *Ann Thorac Surg* 2003; **75**: 1792-6.

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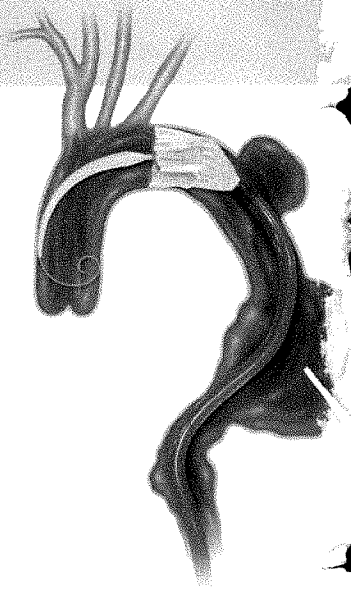
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Zenith TX2 の詳細情報については、下記の営業所にお問い合わせいただくか、www.cookmedical.com/jp/tx2 をご覧ください。

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製造販売元
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ラウンドクロス元代々木ビル
TEL: 03-3468-9911 FAX: 03-3485-2126

販売名: Cook Zenith TX2 TAA エンドバスキュラグラ
承認番号: 22300BZX00147000



sclerosing agent for varicose veins

Polidocasklerol®

0.5% Inj. 2mL • 1% Inj. 2mL • 3% Inj. 2mL

<polidocanol>

Powerful drug, Prescription drug ^{Note)}

Listed on the NHI reimbursement price list

Note) : Caution : Use only according to prescription.

Please refer to the package insert for further prescription information, precautions for use including Dosage, Administration, Warning, Contraindications.



Sales in Japan :
ZERIA Pharmaceutical Co., Ltd.
10-11 Nihonbashi Kobuna-cho, Chuo-ku
Tokyo 103-8351, Japan
TEL (03) 3661-1039
<http://www.zeria.co.jp>

Marketing authorization holder in Japan :
Sakai Chemical Industry Co., Ltd.
1330-1 Matsugaoka Nakamachi,
Kawachinagano, Osaka 586-0006, Japan
<http://www.sakai-chem.co.jp>

Manufacturer [For more information] :
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drug price list

Caduet® Combination
Tablets

Amlodipine Besilate • Atorvastatin Calcium Hydrate

Powerful drug, Prescription drug
Caution-Use only pursuant to the prescription of physician, etc.

※ Please refer to the package insert about RELATIVE CONTRAINDICATIONS,
INDICATION, DOSAGE AND ADMINISTRATION and PRECAUTIONS.

1tab 2.5m
2tab 2.5m
3tab 5mg/
4tab 5mg/

Manufactured and Distributed
Pfizer Japan Inc.
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Tokyo 151-8589, Japan
Inquiries regarding drug information:
Drug Information Center

Co-promotion
Astellas Pharma Inc.
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